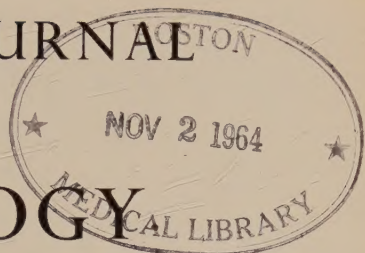


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LIVER BIOPSY IN ECZEMA AND OTHER DERMATOSES.*

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THIS is the first report of investigations we have made at Lille during the past fifteen months on the liver in 73 cases of skin disease.

Specimens of liver were removed by needle biopsy, with only 2 failures. Forty-four of these patients had eczema and can be divided into four groups, viz. :

- (i) Atopic dermatitis (6 cases).
- (ii) Sensitization dermatitis (21 cases). Eight patients had evidence of hepatic disease (5 alcoholic, 2 infective and 1 cardiac).
- (iii) Eczema intolerant of treatment with numerous external and internal remedies (10 cases).
- (iv) Dermatitis from gold (6 cases) and arsenic (1 case).

The remaining 29 cases included Dühring's disease, pemphigus, lupus erythematosus, psoriasis, lingual amyloidosis and mycosis fungoides and were too few to permit us to come to any definite conclusions.

In addition to classical staining methods, viz., Masson's trichrome for collagen and Best's technique for glycogen, we used Wilder's method to demonstrate the argentaffin *gitterfasern*. Radial reticulum fibres follow the course of the liver sinusoids and are united by transverse fibres. In the portal areas they lie on large collagen bundles. They may become frayed or broken into fine granules, or may thicken. In addition to this histological study we made hepatic function tests in all cases, and numerous blood investigations. In some cases we tested the function of the autonomic nervous system.

* Based on a paper read by Professor Huriez before a joint meeting of the Société française de Dermatologie et de Syphiligraphie and the British Association of Dermatology, held in London in July 1956.

Our results may be compared with those of Dogliotti, Banche and Angela (1954) of Turin, who are the only authors who have published results of liver biopsies in dermatological cases.

ECZEMA.

Dogliotti *et al.* found hepatic lesions in acute cases only. They described anisocaryotic and anuclear cells, balloon cells, and in some cases nuclear inclusions, showing as little rods with the chromatin arranged at the periphery. They described reinforcement of the connective tissue bundles in the portal areas with fragmentation of reticulum fibres. In some specimens they saw fatty vacuoles and concluded that early toxic hepatitis was present in 12 of their 14 cases. Liver function tests were abnormal in only 4 of their patients. They found no abnormality of the reticulum fibres in chronic eczema.

We studied the liver in 44 patients.

(i) In 6 cases of atopic dermatitis, no histological lesions were found and liver function tests were normal; the liver was intact.

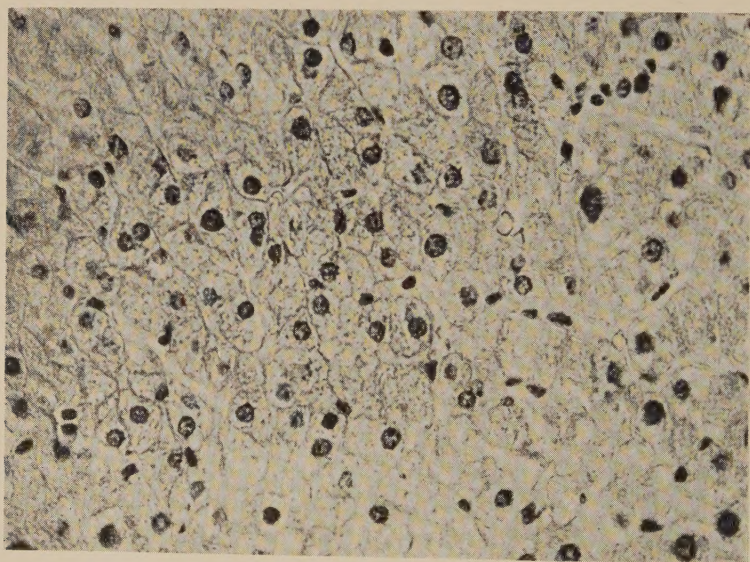


FIG. 1.—Sensitization dermatitis. Liver biopsy showing slight anisocaryosis.

(ii) In sensitization dermatitis, only 4 of 13 cases showed histological changes (vacuolated nuclei and anisocaryosis, Fig. 1) or disturbance of function. Liver disease in the 8 patients already mentioned no doubt predisposed them to sensitization dermatitis, protracted its duration and rendered treatment difficult.

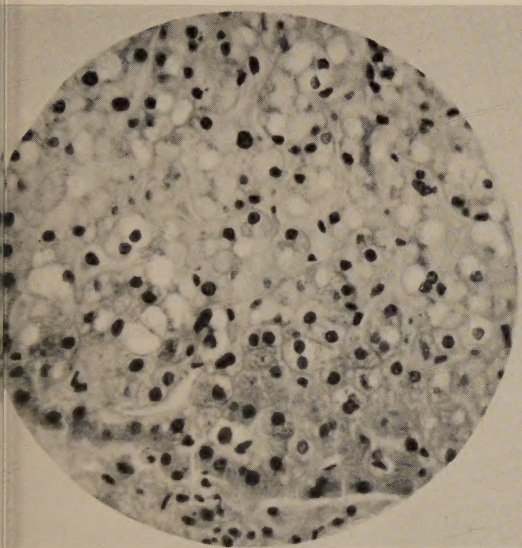


FIG. 2.—Eczema with polyvalent sensitivity. Liver showing diffuse fatty infiltration and anisocaryosis.

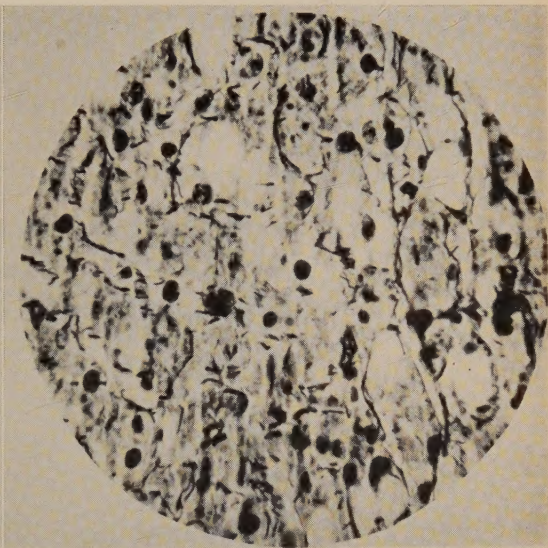


FIG. 3.—Eczema with polyvalent sensitivity. Numerous reticulum fibres broken or absent, particularly near fatty cells (Wilder's method).

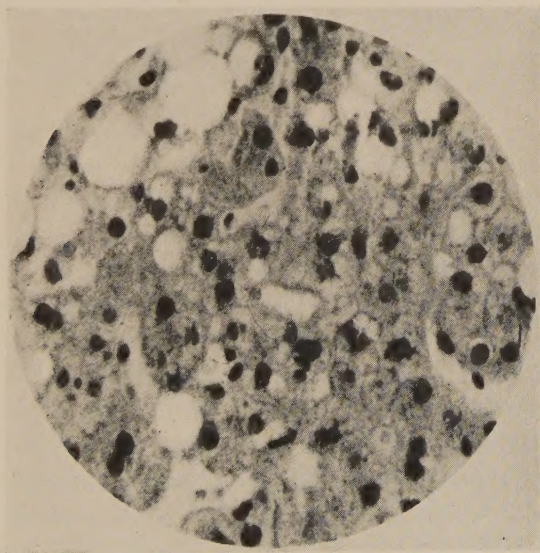


FIG. 4.—Gold dermatitis. Liver showing fatty change, anisocaryosis and pycnotic nuclei.

(iii) In cases of eczema with polyvalent sensitivity, liver lesions were frequent and severe (fatty vacuoles, anisocaryosis, vacuolization of nuclei, Fig. 2; alteration of reticulum, Fig. 3). They occurred in 60% of patients sensitive to numerous drugs used externally or systemically, although hepatic function tests nearly always proved normal.



FIG. 5.—Gold dermatitis. Thickened broken reticulum.

(iv) In dermatitis from gold and arsenic, hepatic changes were constant and severe, showing as fatty vacuoles, anisocaryosis, pycnosis and vacuolized nuclei (Fig. 4). The argentaffin reticulum was frayed or broken into granules (Fig. 5); some fibres were thickened. Gold was detected in the urine in all cases by the technique of Merville, Verhaeghe and Dequidt. The metal was detected twice in the liver and skin by the method of Burchardt and Michaelis (Fig. 6). For arsenic, we used the silver process of Schumacher and Janecso.

During the war, we observed the liver in two fatal cases of arsenical erythrodermia. Gross necrosis resembling that in chloroform poisoning was present in one case; in the other there was a marked shrinkage of Küpffer cells. Fixation of metals by Küpffer cells was demonstrated long ago in experimental animals. Gonin's (1954) observation is most instructive: He demonstrated lifelong persistence in the liver of thorotrast, a substance used in arteriography. Thirteen years after injection, particles of thorotrast were still present in the liver.

In patients suffering from dermatitis from heavy metals we found marked disturbance of autonomic nervous function. Sympathetic paralysis was present when the patient arrived in hospital and after treatment with B.A.L. there was overactivity of the sympathetic. In healthy patients, drugs are well tolerated because the reticulo-endothelial system, and the liver K  pffer cells especially, ensure a blood concentration which is not toxic to tissues in general

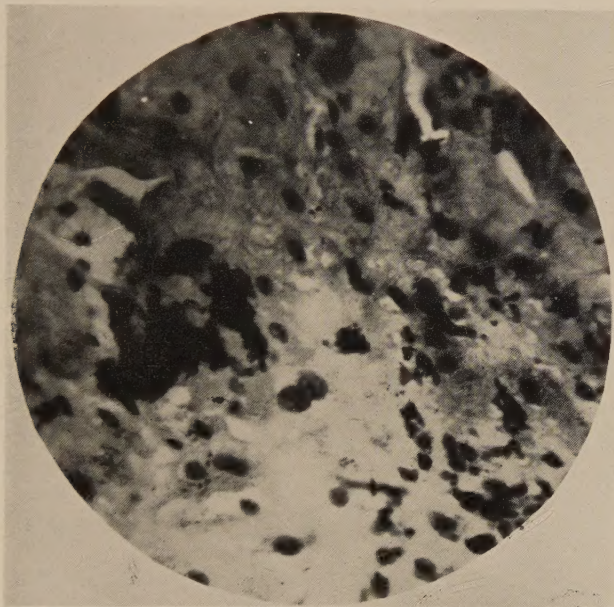


FIG. 6.—Gold dermatitis. Liver showing gold contained in Kupfer cells.

and the autonomic nervous system in particular. In serious disorders such as arsenic and gold dermatitis we showed that there is deterioration of the liver with impregnation of K  pffer cells and skin histiocytes. This results in paralysis of the autonomic nervous system and infection of the skin and deeper tissues.

Histological study of the liver in these cases of eczema also enabled us to assess the real value of hepatic function tests. Only 9% of cases showed positive turbidity tests whereas histologically 31% were slightly altered and 19% badly affected. Electrophoretic studies revealed 13 cases in which the albumin-globulin ratio was reduced to 0.8. Only 9 cases were normal in this respect. Hyperglobulinaemia is particularly common in sensitization dermatitis in which it merely indicates infection and is not a sign of hepatic disturbance. In fact, only liver biopsy can be relied upon to inform us of the actual state of this organ.

Summary.—Liver biopsy in 44 cases of eczema permits us to conclude the modest rôle of the liver in most cases of atopic dermatitis and sensitization eczema. Such forms of eczema are, nevertheless, more frequent and serious in patients with liver lesions.

In contrast, the liver is often abnormal in cases of eczema sensitive to manifold topical and systemic treatments.

Finally, hepatic changes are constant and severe in eczema and erythrodermia due to gold and arsenic, which should be regarded as toxicodermias.

VARIOUS DERMATOSES.

It is impossible to come to definite conclusions in this series which comprised 1 case of dermatitis herpetiformis, 2 of pemphigus, 2 of mycosis fungoides, 1 of lingual amyloidosis, 2 of chronic lupus erythematosus and 21 of psoriasis. It seems worth while to record our findings and to compare them with those of Dogliotti *et al.*, who studied 1 case of dermatitis herpetiformis, 3 of pemphigus, 2 of acute lupus erythematosus, 3 of dermatomyositis and 9 of psoriasis.

In their case of dermatitis herpetiformis, Dogliotti *et al.* found fatty vacuolization of the liver in the first biopsy, progressively less after treatment. In our case, which was fatal, liver biopsy showed marked fatty and inflammatory infiltration with early cirrhosis and marked changes in the reticulum fibres.

One case of pemphigus showed only slight liver changes. The other showed slight fatty change, early fibrosis and moderate lesions of the reticulum fibres which were broken into frayed strands. This case had survived for five years under treatment with terramycin and cortisone. In Dogliotti's series, 3 cases showed thickening of reticulum fibres which later became fragmented. They stressed the progressive increase of fatty infiltration. Charpy and Bolgert also observed fatty hepatitis post mortem.

In one case of chronic lupus erythematosus we found no changes apart from slight anisocaryosis. He had had this disease since 1951 but had been treated with 20 g. of chloroquine. In the other case lesions had been present on the face since 1945 but there were no visceral lesions. The liver changes, however, were very marked and consisted of fatty necrosis, anisocaryosis and separation of the reticulum fibres. Dogliotti *et al.* recorded this change in the reticulum in 2 cases of acute lupus erythematosus.

In psoriasis, Dogliotti *et al.* noticed portal fatty change. In some cases there was necrosis with toxic hepatitis and nuclei showing peripheral arrangement of chromatin; fibrosis was present in a case of acute exanthematic psoriasis. We made biopsies in 21 cases. Two patients were heavy drinkers with alcoholic hepatitis; the others comprised 11 adults and 8 children. The liver in the adults showed various degrees of fatty change, necrosis, anisocaryosis and vacuolated nuclei; in 2 cases there was cirrhosis and thickening of the reticulum

fibres. These changes seemed to be related to the age of the patient, the duration of the skin lesions and to past treatment with potent drugs such as arsenic, bismuth, gold and mepacrine. In children, liver changes were less. A 13-year-old girl had had hereditary psoriasis for a short time, but had had neither treatment nor disease of the liver. Her liver biopsy, however, showed diffuse fatty infiltration and annular fibrosis (Fig. 7). Three children showed nuclear vacuoles in the periportal zones (Fig. 8) of a type which Cazal and Mirouze believe to be carbohydrate. It is not impossible that these hepatic lesions in psoriasis may be related to the disturbances in fat and carbohydrate metabolism which have been found by many authors.

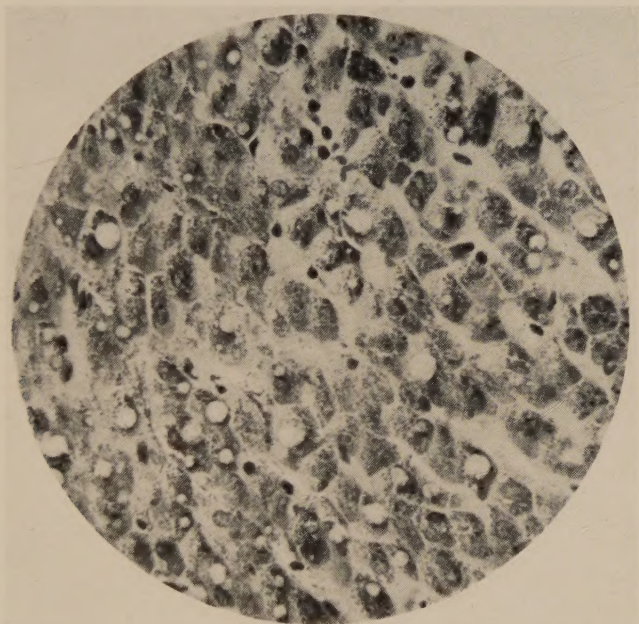


FIG. 7.—Psoriasis in a girl of 13. Diffuse fatty infiltration, glycogen normally distributed. Best's carmine.

We must be more careful in the interpretation of the liver biopsies in our two cases of mycosis fungoides. One case presented as erythrodermia but its premycotic nature was suspected after biopsy of a lymph gland. The liver presented fatty infiltration and non-specific lesions of the reticulum fibres. In contrast, in a case with tumours we found a portal and perivascular histiocytic and monocytic infiltration similar to that observed by Dogliotti *et al.*, suggesting that the disease process had reached the liver.

No liver changes were found in a case of macroglossia; lingual amyloidosis led to the discovery of multiple myeloma with marked plasmocytosis of the bone marrow.

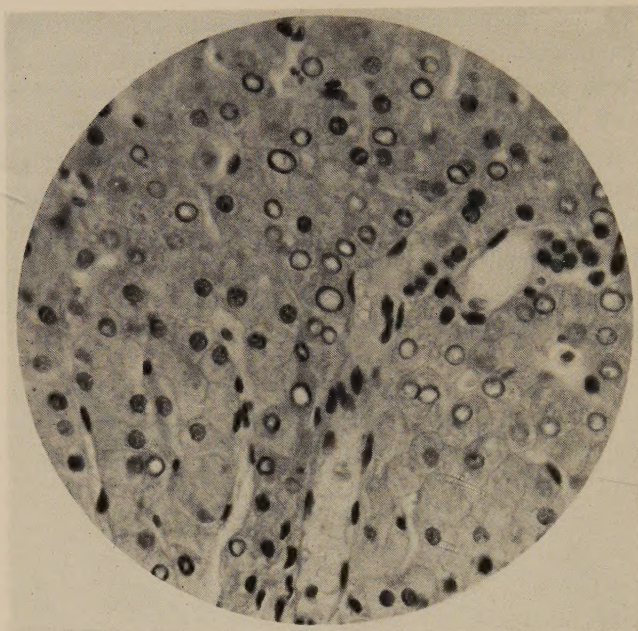


FIG. 8.—Psoriasis in child of eleven. Vacuolated nuclei.

CONCLUSION.

The skin is the mirror of many infections and of numerous metabolic disorders. Liver biopsy helps us to accept or reject those theories concerning the rôle of the liver in the genesis of certain skin diseases.

It should be emphasized that such biopsies may reveal antecedent or concomitant hepatic lesions which may not be responsible for the skin disease. They may be the consequence of earlier infections or intoxications, sclerosis resulting from these lesions, or of senescence.

To be prudent, we have attributed to alcohol any such changes in intemperate patients. However, the frequency and severity of hepatic changes in temperate subjects, particularly in young women, must be significant. Much more investigation is necessary before we can be certain.

Liver biopsy is destined to render appreciable service in the future. It will be of use in cases where the diagnosis is equivocal, in prognosis and in the evaluation of treatment.

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SUBACUTE HYPODERMIC NODULES OF VASCULAR ORIGIN.

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INTEREST shown during recent years in the relapsing nodular panniculitis of Weber and Christian has obscured the problem of subacute hypodermic nodules of vascular origin which are, in fact, of much greater practical importance.

This communication is based on 13 cases of hypodermic nodules showing marked vascular changes seen last year at the Broca Hospital by my colleagues, Drs. Richon, J. J. Meyer de Schmid, Desvignes, and myself. From this series we have excluded 2 cases of primary panniculitis without vascular lesions and 11 cases of post-thrombophlebitic sclerosis of the leg (*hypodermite sclerodermiforme perivariqueuse*), the infiltrated plaques of which have nothing in common with the subcutaneous nodes we are discussing. We have also left out 2 cases of nodular thrombophlebitis of the legs in men; although these bear a clinical resemblance to hypodermic nodules, they are distinguished by being oblong in shape and strictly localized to the veins, the obliteration of larger vessels having little effect on the surrounding fat. Finally, we have excluded the acute hypodermic nodules of erythema nodosum, while bearing in mind that some of the nodules in our patients may undergo recurrent acute attacks and yet run a course which is predominantly subacute.

The remaining group into which our patients fall consists of those subacute nodules which show marked lesions of the subcutaneous vessels and fatty tissue, ranging from simple exudative inflammatory changes to necrosis. Erythema induratum (Bazin) is a typical example. It might be thought easy enough to diagnose this condition—particularly if some of the nodules have ulcerated—and to accept its tuberculous origin. But from the end of the last century, following Audry's first observation, Whitfield, Galloway and others in Great Britain have claimed that there was a non-tuberculous type of erythema induratum. They recognized the following characteristics: A later onset than in Bazin's disease, and the frequent coexistence of peripheral circulatory trouble; a course that is more acute, more inflammatory and more painful; less frequent ulceration; absence of any question of tuberculous aetiology; cure with the relief of vascular stasis by bed-rest. Much more recently, Montgomery and O'Leary have taken up this conception again and refashioned it under the name of "nodular vasculitis", making this an entity of its own, a nodular condition which is the result of a primary injury to the subdermal

blood vessels. The concept of a non-tuberculous erythema induratum was of definite value at the beginning of this century and threw open the door to new aetiological investigations; but to renew the same idea and call it primary nodular vasculitis seems like going up a blind alley.

The study of our cases shows that there are two poorly distinguished groups of subacute vascular hypodermic nodules. Erythema induratum of Bazin retains a certain clinical individuality with its predominance in women, its purplish nodules showing prolonged attacks of activity in the winter and the frequent tendency of the nodules to ulcerate during the more severe attacks. Our first 7 cases fitted in very well with this description. None of the characteristics are constant; pain sometimes occurs (cases 1 and 5); the age of the patient at onset varies from 26 to 57 years (the latter in case 5, a patient with old pulmonary tuberculosis).

The aetiology of these typical cases seems in general to be tuberculous, but one should not accept this explanation blindly. We have seen, with Professor Degos, a case of erythema induratum in which an aerobic streptococcus was recovered from a ground-up nodule. Contrary to general belief, even the histology does not show a typically tuberculous picture in most cases. One frequently sees false tubercles due to *wucherungsatrophie*, a vaguely tuberculoid but non-specific reaction of the fatty tissue. Necrosis is due not to caseation but to ischaemia, because the chief lesion is an obliteration of the large veins and arteries of the subcutaneous tissue. Other evidence of a tuberculous origin rests in guinea-pig inoculation and culture—which are rarely positive—a past history of tuberculosis, and a positive tuberculin reaction—which is the rule. The haemagglutination reaction of Middlebrook-Dubos is generally negative.

If it is difficult to prove the tuberculous nature of Bazin's disease, it is because we are really dealing with a nodular vasculitis in the broadest sense of the term. Peripheral vascular upsets are often present and cold frequently plays a part; the tubercle bacillus attacks the endothelium of the subdermal blood vessels by a process that is probably allergic. This explains why specific anti-tuberculous therapy is often ineffective while vitamin C and vasodilators more frequently succeed. If tuberculosis acts by sensitizing the vessels, there can be no theoretical objection to clinically and histologically typical erythema induratum being due to factors other than tuberculosis. It seems that this may be true particularly in regard to the streptococcus. In the present series cases 6 and 7 showed ulcerated lesions of erythema induratum of the Hutchinson type, but there is reason to suggest a streptococcal origin for the first and, especially, for the second of these cases (Table I). We shall return later to a discussion of the arguments concerned. Thus, even for the most typical case of Bazin's disease, the aetiological problem is not as simple as is usually thought. Investigation should be chiefly directed towards tuberculosis but also towards the possibility of a wide

variety of infections—above all streptococcal—and even in the last resort towards the possibility of an allergic drug eruption. In short, the vascular involvement is the important thing and it is scarcely stretching the point too far to say that the finest example of “nodular vasculitis” is to be found in Bazin’s disease.

In the second of these groups the hypodermic vascular nodules are more inflammatory than in erythema induratum. They present the characteristics that we have mentioned above and which were described precisely by British authors at the turn of the century under the name of non-tuberculous erythema induratum and to which Montgomery and O’Leary gave the name of nodular vasculitis.

In fact, these inflammatory subacute hypodermic lesions are fairly polymorphic, as is seen by the second part of Table I. Some are very like erythema induratum and may ulcerate. The two conditions tend to merge; for instance, cases 7 and 8 could be placed in either category. The histology of case 8, in particular, is very close to that of erythema induratum, with vascular obliteration, but the more inflammatory clinical course and the collarette-like detachment of the epidermis which Professor Degos has described in streptococcal lesions puts it into the second group, and indeed there were further arguments in favour of a streptococcal origin.

Other cases are more superficial, with a more intense dermal involvement and a more acute course. The attacks are often frequent, almost overlapping each other (cases 10 and 13). Subacute inflammatory plaques may be associated with the nodules, which are often small and very variable in number. Briefly then, this second, more inflammatory group of hypodermic nodules which corresponds with the nodular vasculitis of Montgomery and O’Leary shows a very polymorphic picture, considering the uniform modes of reaction of the subcutaneous tissues.

When we come to consider aetiology and pathogenesis the question is much more complex. An abnormal constitutional vascular terrain seems to us to be less common than in typical erythema induratum (cases 7, 11 and 13). Some cases occur in the summer (case 8). A rheumatic diathesis is sometimes manifest (febrile arthralgia and a past history of acute rheumatism in case 12, recurrent arthritic attacks in case 13). We can have no doubt that we are dealing with a vascular condition and not with attacks of isolated panniculitis of the Weber-Christian type.

In case 12, in which there was a past history of joint symptoms, it was possible to reproduce attacks at will with sulphathiazole and sulphapyridine. That it was not a simple case of erythema nodosum induced by drugs is shown by the fact that a subacute inflammatory plaque was present which resolved only some time after suppression of the toxins. In this respect we might add that in a patient suffering from a superficial cord-like thrombophlebitis with a

perivascular reaction in the hypoderm, a rapid end to a two months' old attack came about after leaving off sodium bromide. It seems that these subacute inflammatory reactions of the dermis and subdermis may often be of streptococcal origin, as has been pointed out by Gougerot and Degos. We have been able to show this by culture of the nodules, but the bacteriological evidence is as difficult to obtain as it is in tuberculous cases, and for the same reason; in both cases the mechanism is likely to be allergic in character. Biological and therapeutic tests need cautious interpretation, but the more the evidence the more one can presume from it.

There are two biological tests which can be of value, the intradermal reaction to a stock anti-streptococcal vaccine and the antistreptolysin titre. A search for haemolytic streptococci in the throat can sometimes be useful but it was misleading in case 12, where the attacks were really due to the sulphonamides that she was taking for her recurrent sore throats. In her case the antistreptolysin titre was low (120 units). A more useful example is shown by case 9 where there was a strongly positive (blistering) intradermal reaction to antistreptococcal vaccine and a raised antistreptolysin titre (960 units). As would be expected, sulphapyridine had a rapid effect on the nodules and a course of progressive antistreptococcal inoculations has enabled us to prevent any recurrence up to the present.

At other times interpretation is more difficult. In case 8, for instance, the histological picture was very similar to that of erythema induratum and the intradermal reaction was strongly positive; but the antistreptolysin titre of 240 units was at the upper limits of normal. Antistreptococcal vaccination was followed by rapid cure.

Therapeutic tests obviously need interpretation as well. Following the practice of Degos we gave our patients sulphonamides, particularly sulphapyridine. The immediate result was often good, though only transitory if the focus of infection had not been dealt with. Moreover, streptococcal vascular allergy should theoretically demand antistreptococcal vaccination, the efficacy of which seems to have been particularly striking in three cases (7, 8, and 9).

Whatever the precipitating cause, *peripheral vascular disorders* are very important in many of these patients with hypodermic nodules and call for treatment in which vasodilators have an important part to play.

We appreciate how imprecise and incomplete are these views, as yet unproved. It is possible that certain subacute hypodermic nodules may show no evidence of an infectious or toxic cause; these can be regarded as cases of nodular vasculitis in the narrow sense of the term. There is no doubt that bed-rest and vasodilators offer the best treatment when vascular lesions seem to be primary and, of course, for those cases of thrombophlebitis that involve the large veins. But we think that this applies to only a minority of cases and should be considered only when one has eliminated, by a searching investigation, all

those blood-borne factors which may excite vascular reactions in a favourable soil.

Thus the concept of nodular vasculitis seems to us to lose much of its importance ; if one accepts it in the narrow sense as a primary vascular disease of the hypodermic tissues, it is a diagnosis made by elimination and, we believe, an exceptional one. If, on the other hand, one accepts it in the broad sense, the concept of nodular vasculitis merely separates one group of conditions from cases of primary panniculitis of the Weber-Christian type. Here we agree with Vilanova that nodular vasculitis then becomes merely a synonym for what we call subacute vascular hypodermic nodules. As such, it stresses the vascular lesions and to this extent is valuable. But it is then no more than a very general term, a chapter heading ; the start and not the end of those aetiological investigations which must remain our task.

ANGIOMA SERPIGINOSUM.

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ANGIOMA SERPIGINOSUM was first described by Jonathan Hutchinson in 1889 and called by him "A peculiar form of serpiginous and infective naevoid disease". It was a form of angioma usually developing in early childhood, the basic lesion being a superficial vascular dilatation, the condition continuing to spread peripherally by the formation of satellite spots. His first case, as reported in his *Archives of Surgery* (1889-90) was that of a 15-year-old girl in whom a lightly marked port-wine stain was noted on the back of the arm soon after birth. After some years it began to spread and here I quote from Hutchinson's original description: "A careful inspection of the plate will show that the mode of advance is somewhat peculiar and that it has not been by a continuous edge. It would appear as if little satellite spots had been produced, which had spread into circles, and, by gradually advancing by infective edges, had coalesced, producing the irregular pattern, which is here displayed" (Fig. 1). Speaking of these spreading circles he later says: "They were extremely superficial and it was even difficult to be sure, whether or not they left any state of scar behind them. I have, however, no doubt that such was their tendency and that in some places a slightly marked superficial scar could be demonstrated. The enlarged capillaries could be partially emptied by pressure, but not wholly, and in many places little tufts were distended by deeply-purple venous blood, which could not be pressed out".

In the second volume of his *Archives* (1890-91) Hutchinson described two more cases, one being that of a 19-year-old male (Jamieson's case) with the affection on the right arm of about 4 years' duration and the other being a moulage of a case of Lassar's which was that of a 3½-year-old girl with the forearm affected and also a few similar patches on the cheeks and ears, having been first noticed at the age of 9 months. In the third volume (1891-92) he described a case shown to him by Tay as the fourth typical example which he had seen to date. The patient was a 12-year-old girl, the condition having started at the age of 2 and affecting the right leg "extending continuously from the heel to the knee and reappearing as a separated patch on the front of the thigh about a hand's breadth above the joint. The back of the limb was covered over with minute dots of deep red or almost purplish tint . . . They were closely placed but for the most part discontinuous with each other and not arranged in rings or in any other definite kind of grouping . . . There

was no evidence of their having undergone any retrogressive changes and not the slightest trace of a scar could be detected". In the most recently affected area the dots were not nearly so closely placed. Thus scarring was completely absent in three of Hutchinson's cases and slight, if at all, in the fourth.



FIG. 1.

Wise (1913) believed that Hutchinson had described a fifth case in 1889 which he had called *lupus marginatum*. This was a young boy, with patches affecting the face, which were abruptly margined with delicately tuberculated or lichenoid borders and some scarring. The left arm was also affected, with a linear distribution, again with a finely tuberculated border and scarring in the centre. This, however, differs in many respects from Hutchinson's other cases and the fact that 3 years later he considered Tay's case to be the fourth he had seen, indicates that he did not include this case of *lupus marginatum* in the same group.

Of these four cases the histology was studied in only one, that of Jamieson's patient. Here the epidermis was found to be normal although processes were seen to run down between the cones deep into the corium. The vascular loops at the apices of the papillae were dilated into wide spaces, some of which contained blood. Hutchinson interpreted this as a very superficial capillary naevus spreading by the formation of satellites, which presented on the skin as the isolated puncta.

Hutchinson's use of the term "infective" and his reference to the similarity of this condition to lupus may have been partly responsible for the subsequent confusion over the criteria necessary for the diagnosis of angioma serpiginosum. In describing his first case he mentioned that the formation of the little tufts distended with deeply purple venous blood which could not be pressed out, along with the tendency to serpiginous spread and the production of "satellites", closely resembled what is seen in the disease which he called "lupus lymphaticus" and which we now know as lymphangioma or haemolymphangioma. Commenting later on Lassar's *moulage* he again refers to the similarity to lymphangioma: "there is no doubt that in the one case the morbid process is that of a lymphangioma and in the other of an angioma but these names are those of pathological anatomy only and do not comprise any reference to the clinical features of the malady. It is in the latter that the lupoid characters appear". He also stresses later he did not consider that "lupus lymphaticus" was the same as either lupus vulgaris or lupus erythematosus. He further clarifies the position during the report of his fourth case by saying: "when I speak of this case as being only the fourth which I have seen, I refer to uncomplicated and closely similar cases. As part of the phenomenon of lupus lymphaticus or infective lymphangioma the cayenne pepper grains are constantly present, so also do they occur as part of certain forms of port-wine stain". He considered therefore that angioma serpiginosum was allied on the one hand to non-infective naevus and on the other to the infective lupus lymphaticus although he considered that it should be a separate group. White (1897), Walsh (1898) and Radcliffe-Crocker (1903) all stressed that Hutchinson by the use of the term "infective" intended to lay stress on the mode of spread by satellite spots at the periphery rather than to infer that the condition was caused by any micro-organism.

The name angioma serpiginosum by which we now know the condition was given to it by Radcliffe-Crocker in 1893. He considered that the diagnosis should scarcely offer any difficulty; the fact that it started some time after birth at once showed it to be no mere birthmark and "its punctiform character in groups, rings, lines or single dots and tendency to spread in an annular manner with continual formation of fresh foci beyond the main patch, stamps it as something peculiar".

Study of later reports in the literature reveal a wide divergence of opinion

as to the criteria for diagnosis. Michelson (1935) in the discussion of O'Leary's case said that he had no clear-cut conception of Hutchinson's angioma serpiginosum despite the descriptions of Radcliffe-Crocker and Wise. In an attempt to clarify the position I here report eleven cases seen at St. John's Hospital and the Hospital for Sick Children, Great Ormond Street. Dr. C. H. Whittle also kindly allowed me to examine two of his patients (Cases 10 and 11) and include them in this series.

CASE REPORTS.

Case 1.—A girl aged 9 years.

The condition appeared on the right leg at the age of $3\frac{1}{2}$, although the exact site of onset was uncertain. There was, however, a gradual spread which was still continuing when she was first seen on 2.vii.56 at the age of 9 years. At that time it was found to extend widely over the posterior aspect of the leg, from the buttock down to the lower third of the calf. The eruption consisted entirely of dark violaceous angiomatous puncta either in linear, serpiginous or gyrate groups and elsewhere as scattered discrete lesions. The appearance was identical with that seen in Case 3 (Fig. 3). Slight fading of colour on diascopic pressure was obtained in a few areas but the majority of the lesions were unchanged by pressure. Disappearance of lesions during an observation period of 6 months did not take place and apparently had not done so previously.

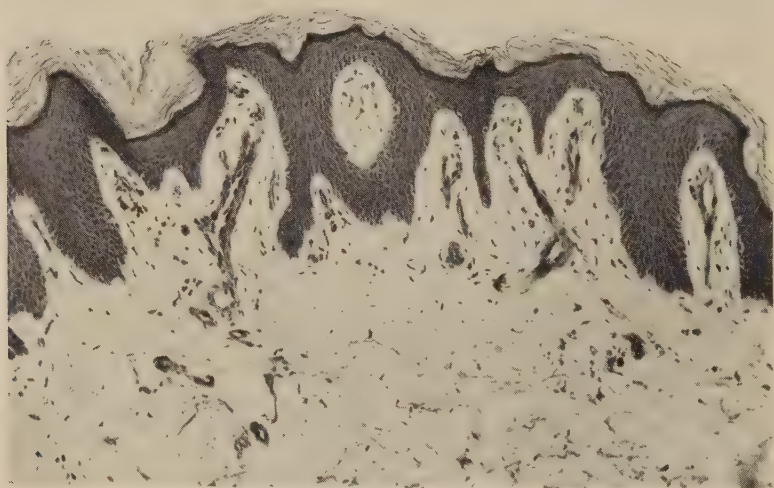


FIG. 2.

Case 2.—A girl aged 9 years.

The condition was first noticed on the medial aspect of the left thigh at the age of 4 years. Gradual spread took place during the next two years, mainly over the antero-medial aspect of the thigh and down round the medial aspect of the knee on to the front of the lower leg. The condition has been stationary for the last 3 years

except for the development of a small similar group of lesions on the right thigh. The colour in most areas faded partly on compression, the lesions consisting mainly of minute telangiectases with numerous red and violaceous puncta. During a period of 18 months clearance of lesions was not observed.

The histology was reported on by Dr. H. Haber as showing hyperkeratosis of the basket-weave type, acanthosis and elongation and fusing of the rete pegs. The papillae were elongated and oedematous. The papillary body contained a few small vessels with thickened walls (Fig. 2).

Case 3.—A girl aged 11 years.

The lesions were first noticed on the back of the right calf at the age of 6 years, gradually spreading to involve large areas, and to the thigh as far as the junction of the middle and upper third of the buttock (Fig. 3). Some years after the start, the

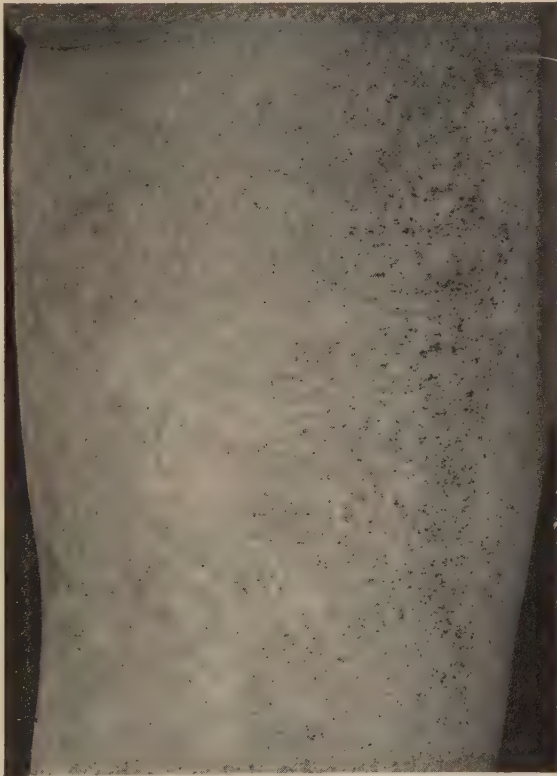


FIG. 3.

left leg also was affected in the same distribution, although the lesions were fewer. The development of fresh puncta has continued over a period of observation of 18 months, since her first attendance on 14.vii.55, the spread over the buttocks being observed to take place during this interval. There is also a slight similar involvement of the posterior aspect of the left upper arm. In this case the dark violaceous puncta predominated with only a slight dusky background in a few areas. Disappearance of lesions was not observed but partial obliteration of colour on

diascopic pressure was obtained in some areas. Bleeding and clotting time and platelet count were normal, although Hess's capillary fragility test was moderately positive.

Case 4.—A girl aged 6 years.

The first skin change was noticed at the age of 3 years. When she was first seen on 4.vii.55 at the age of 6 it was found to involve extensive areas of the right lower limb, most marked over the antero-lateral aspect of the lower leg, spreading up over the knee to the middle third of the thigh anteriorly and down to the dorsum of the foot and medial aspect of the sole. The site of onset and rate and mode of spread were uncertain but there had been little if any alteration during the year prior to her first attendance. During a subsequent year under observation the lesions did not alter. In many areas there was a background of diffuse dusky erythema with numerous dark violaceous puncta, the peripheral lesions being isolated puncta in variations of grouping on otherwise normal skin. Some degree of fading was produced by diascopic pressure but many of the darker coloured lesions were unaffected by pressure.

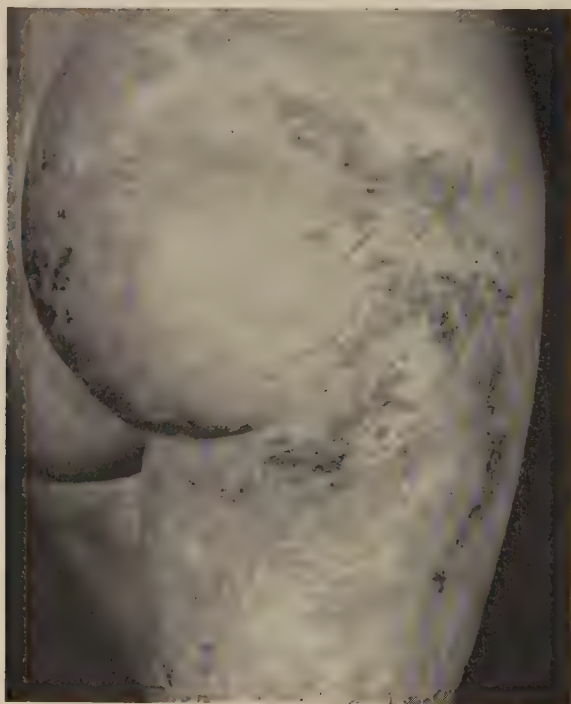


FIG. 4.

Case 5.—A girl aged 5 years.

A reddish discoloration of the skin of the left buttock was first noticed at the age of two weeks but the mother was not certain whether anything abnormal had been present at birth: within a few weeks both calves were also seen to be affected. Fairly rapid spread took place during the first year of life to extensive areas on the back of both lower limbs, the right being more affected than the left, particularly

over the buttocks, upper thigh and calf (Fig. 4). In this case also there was a dusky erythematous background containing numerous darker violaceous puncta with partial fading of colour on compression in some areas, but elsewhere no change was produced by pressure. Numerous discrete puncta were also noted over the right pinna and on the right forearm, these having appeared during the first year or two of life. Where the dorsum of the right foot was involved the clinical appearance was identical with that of the ordinary naevus flammeus.

Case 6.—A girl aged 9 years.

The first skin abnormality was noticed at the age of $3\frac{1}{2}$ on the left calf, and spread over this area during the following year. There was then little activity until the age of 7 years when angiomatous puncta were first noticed on the back of the left thigh, and a gradual progression has taken place down towards the calf and more recently on to the buttock. Observation over the last year has confirmed the appearance of fresh puncta although the development of these new lesions has been by no means rapid. Although the basic lesion was again a dark violaceous punctum there was in addition, in some areas, a background of dusky erythema and some of the lesions were found to be more linear than punctiform. In only some areas was fading on compression obtained. The histology was reported on by Dr. H. Haber as showing conspicuous capillary vessels as seen in cases of naevus flammeus with slight round cell infiltration surrounding these vessels.

Case 7.—A girl aged 16 years.

This case was first shown by Musso (1953) to the section of dermatology of the Royal Society of Medicine. At that time the condition involved the antero-medial aspect of the left thigh, consisting of purplish-red pin-point size flat angiomatous lesions which were either discrete or in groups of irregular shape. They were not emptied by pressure. A very small group of similar lesions was also present on the front of the right thigh. The condition had first appeared at the age of 6 years, gradually spreading until 12 years of age, remaining stationary for the next 3 years when the puncta gradually began to disappear. When she was seen again on 9.iv.56 at the age of 16 years they had all virtually cleared although a fair number of discrete puncta were found scattered about the previously affected site; they were insufficient to form any regular grouping and only discernible on close inspection.

Case 8.—A woman aged 45 years.

This case was first presented by Wigley (1946) to the section of dermatology of the Royal Society of Medicine. The condition was first noticed about the age of 11 years on the outer aspect of the right upper arm, and gradually spread over the years to involve extensive areas of the trunk, thighs and to a less extent of the face and neck. Since 1945 areas of punctiform lesions have cleared spontaneously especially from the originally affected site of the right arm; this clearance has also been noticed to a variable degree in all affected areas. Fresh lesions are still appearing.

In most areas the only lesion is a dark violaceous punctum grouped in variable patterns and present on the sides of the neck, cheeks, and upper eyelids, on both upper limbs and thighs, and on the shoulders and the abdomen. On the abdominal skin there is a background of erythema in some areas and also over the front of the right thigh where it is of a more dusky hue. This background colouring is compressible, but the puncta are unaffected by pressure. Four small areas on the right arm were treated with radium plaques in 1944 and numerous puncta are present in the resultant atrophic scars which the patient is quite certain first developed some years after the radium treatment.

In 1946 Freudenthal reported on the histology as showing that there was in the papillary body a considerable number of dilated capillary vessels, mostly filled with

red blood corpuscles, there being hardly any cellular infiltrate around these vessels. A second biopsy in 1956 was reported on by Dr. H. Haber as showing the only abnormality to be a number of widely dilated capillary vessels in the papillary area, some of which were filled with blood.

Case 9.—A man aged 63 years.

This man attended hospital with discoïd eczema and it was also noticed that he had a linear eruption over the upper part of the right arm, extending posteriorly on to the shoulder. It was composed of dark red puncta with a slight erythematous



FIG. 5.

background in some areas. These puncta were not compressible. It was thought to have developed about the age of 14 years but its subsequent progression was uncertain. On histological examination Dr. H. Haber again reported that there were no abnormal findings other than numerous dilated vessels in the papillary layer, lined by endothelium, with thickened walls. The perivascular collagen was thickened and stained deep red with eosin (Fig. 5).

Case 10.—A woman aged 23 years.

This patient had a linear grouping of violaceous puncta on the medial aspect of the right upper arm which had first been noticed at the age of 8 years, the rate of subsequent spread being uncertain. None of the lesions had disappeared and a few fresh ones might have developed during the last 4 years. The puncta were not compressible.

Case 11.—A girl aged 17 years.

This girl was thought to have had a few small red patches on the left buttock in infancy with some affection of the skin of the back of the left thigh during the first few years of life. Since the age of 11 years, however, the condition has been spreading and is still doing so.

The disorder involves extensive areas of the left buttock, back of thigh and calf. Over the thigh the lesions are practically all dark violaceous puncta, these punctiform lesions also being present in the other areas but on the calf have a background of dusky erythema. There is a variable degree of fading of colour on compression, most marked in the areas of dusky erythema.

CLINICAL FEATURES.

In these eleven cases the basic lesion was an angiomatous punctum varying in colour from red to deep purple; they may reach the size of a pinhead but usually many smaller puncta are also present requiring a lens for adequate identification. In some cases this may be the only type of lesion present (Cases 1, 7 and 10). They are most characteristically found in every case at the periphery of the affected areas, where they were called by Hutchinson the "satellite spots". In some cases there is a variable degree of background erythema which may be dusky in colour and at times accompanied by small groups of minute linear telangiectatic vessels. In some areas the minute puncta are grouped, while elsewhere they may be isolated, singly or in twos or threes in areas of otherwise normal skin. Disappearance on compression varies from case to case but as a general rule the darker coloured lesions are not emptied by diascopic pressure, but in other areas, some degree of blanching may result.

The fact that the dark violaceous spots (puncta) are often unaltered by diascopic pressure raises the question whether the spot is a dilated vessel or a petechial haemorrhage. The puncta, however, always remain discrete and well defined; they bleed readily when pricked, and the stages in the development of petechiae from bright red to brown and yellow are not seen.

The tendency to form various patterns, which may be serpiginous, gyrate or linear appears to depend more on the production of new lesions than due to spontaneous disappearance of others.

In 90% of the cases reported here the patient was a female, a similar percentage to others reported in the literature in this country (Table III). It is usually first noticed before the age of 16 years (Table I . . . 100%; Table II . . . 79%), commonly in the early years of childhood. A capillary angioma may be present at birth but this is unusual. There is a marked tendency for the lower limbs to be affected, often in a unilateral distribution. In most cases the condition is confined to one or two limbs (Table I . . . 82%; Table II . . . 74%), but affection of extensive areas of the body surface can occur (Case 8) and this was also commented upon by Parkes Weber in the

discussion of Goldsmith's case (1939). In the first few years there is a tendency towards gradual progression and the development of new lesions, but at any time there may be a quiescent stage which may last for some years, only for active production of puncta to start again. As in Case 7 the lesions may suddenly all start to disappear spontaneously over a period of some months. In Case 8 the pattern of involvement of the skin has been continually changing over the years, some areas clearing while fresh puncta develop elsewhere on previously unaffected skin. Parkes Weber (1946) and others have also noted this characteristic of spontaneous cure. Residual atrophy has been described although I have not personally observed it and the absence of any scarring has been stressed frequently in other reported cases.

It may be that there are two types of angioma serpiginosum, one in which the eruption is formed entirely by puncta and the other in which numerous puncta are present but where there is also a background of erythema. Disappearance of lesions has occurred so far in two cases of this series both of which were of the first type.

TABLE I.

Case number.	Sex.	Age (years).	Age at onset (years)	Distribution.
1	F.	9	3½	Leg (R.).
2	"	9	4	Leg (R and L.).
3	"	11	6	Leg (R. and L.), Arm (L.).
4	"	6	3	Leg (R.).
5	"	5	3½	Leg (R. and L.), Ear (R.), Arm (R.).
6	"	9	3½	Leg (L.).
7	"	16	6	Leg (R. and L.).
8	"	45	11	Face, trunk and limbs.
9	M.	63	14	Arm (R.).
10	F.	23	8	Arm (R.).
11	"	17	11	Leg (L.).

TABLE II.—Cases Reported in the British Literature.

Case reported by	Sex.	Age (years).	Age at onset (years).	Distribution.
Hutchinson (1889-90)	F.	15	Infancy	Arm.
" (1890-91)	M.	19	15	Arm (R).
" (1890-91)	F.	3½	1½	Arm.
" (1891-92)	"	12	2	Leg (R).
Radcliffe-Crocker (1894)	"	28	2	Face.
Morris (1896)	"	30	18	Leg (R and L).
Roberts (1897)	"	15	4	Leg (R and L).
White (1897)	"	44	20	Face, trunk and arm.
Hutchinson (Jnr.) (1907)	"	12	2	Leg (L).
Morris and Dore (1912)	"	"	"	"
Whittle (1950)	"	24	2	Arms, legs and trunk.
Sequeira (1912)	"	20	2	Arm, neck and trunk.
Pernet (1914)	"	15	13	Arm (L).
Gray (1919)	"	4	Birth	Leg (L).
Little (1921)	M.	12	2	Leg.
Sequeira (1925)	F.	34	19	Leg (R and L).
Parkes Weber (1927)	"	24	22	Arm (R).
Barber (1931)	"	4	2	Trunk.
Goldsmith (1939)	"	20	7	Leg (R), Arm (L).
Musso (1953)	"	11	5	Leg (R.)

TABLE III.—*Comparison of Tables I and II.*

Table	Number of cases.	Percentage of females.	Onset before the age of 16 years (%)	Limbs only affected (%)	Legs only affected (%)
I	11	90	100	82	53
II	19	90	79	74	42

HISTOLOGY.

The absence of histological studies of the cases reported in the past has perhaps played a large part in the uncertainty as to the criteria necessary for diagnosis: this young age group does not lend itself to adequate histological investigation and in this series biopsy was carried out in only four cases (Cases 2, 6, 8 and 9). In cases 8, 9, and 6 the histological appearances were identical, there being present in the dermis, especially in the subpapillary layers, numerous dilated capillaries, some with thickened walls; any cellular infiltrate, if present, was minimal (Figs. 2 and 4). No hæmosiderin was shown to be present. The epidermis was virtually normal.

This histological picture is identical with that described by Hutchinson (1889), Roberts (1897), Hutchinson (Jnr.) (1907), Sequeira (1912), Goldsmith (1939) and Whittle (1950). Wise (1913) however lays stress on epidermal changes and the presence of a marked cellular infiltrate in the dermis; his interpretation has been fairly widely quoted. He says however, "... The question arises, are we dealing with what has been called Angioma Serpiginosum or with a disease, hitherto unknown?" The only histological reports he considered to be of value were those of Roberts, Jamieson (Hutchinson's second case) and Sequeira. Jamieson found the epidermis to be normal and in addition "... vascular loops at the apices of the papillae were dilated into wide spaces". He makes no mention of any inflammatory condition and regarded angioma serpiginosum as a "very superficial capillary naevus". Roberts described cavernous vascular spaces in the papillary layer and stated that there was no inflammatory reaction and none but mechanical changes in the epidermis. Sequeira found that the epidermis was normal and that the capillaries and most of the venules of the deeper layers of the dermis were engorged, there being no infiltration of free cells. Whittle's case (1950) was first shown to the section of dermatology of the Royal Society of Medicine by Morris and Dore in 1912 and was clinically identical with his other two cases reported here (Cases 10 and 11). Histologically this showed only thinning and flattening of the epidermis with absence of the interpapillary processes. In addition there was dilatation of the papillary blood vessels with a very slight perivascular cellular infiltration. Goldsmith's case showed only newly formed blood vessels with thick walls. The case reported by Gray (1931) although differing histologically also had one or two unusual clinical features. Of the

four American recorded cases, clinically simulating those described in this report, the histology was carried out in two (Traub, 1932 ; Ringrose, 1950). In Ringrose's case the only abnormality found was that of dilated capillaries in the papillary plexus. Traub reported dilatation and increase in the number of blood vessels ; the connective tissue between the islands of blood vessels was oedematous and showed degeneration but there was no inflammatory reaction. The epidermis was thin and showed but few rete pegs.

Haber (1957) finds that it is not possible to differentiate this histological picture from that seen in other capillary angiomas but supports Roberts's (1897) contention that angioma serpiginosum is not a true angioma but a neurovascular abnormality of normally existing capillaries. Although in Case 2 (Fig. 2) some inflammatory changes were present in the dermis with epidermal change he considered that this could be explained as a reaction to seepage or transudation from the small vessels resulting from their abnormal dilatation. In this case, however, the degree of inflammatory reaction and of epidermal change was very much less than that described by Wise.

Thus the histological picture in angioma serpiginosum is simply that of dilatation and tortuosity of the small capillaries in the subpapillary layer, usually without any inflammatory reaction and with little or no epidermal change.

Wise, however, basing his histological interpretation on his own three cases considered that the condition was a progressive perivascular infiltration of the papillary and subpapillary layers in circumscribed areas, corresponding to the small deep red papules and the rings of the annular lesions. In these areas he found proliferation of the capillaries as in inflammatory tissue with marked endothelial proliferation and swelling. The epidermis over these areas of infiltration showed a high degree of intercellular and intracellular oedema, principally affecting the lower layers of the rete but extending with diminished intensity as far as the stratum granulosum. He also found the lower layers of the rete to be invaded by the lymphocytes from the papillary infiltration ; a few polymorphs were also seen and many of the epidermal cells had undergone hydropic degeneration. The epidermis as a whole was compressed at the highest point of the infiltration and reduced to less than half its normal thickness. The stratum granulosum was thinned or absent. He stressed in addition that he was unable to find any sign of extravasated blood as in a haemorrhagic process or of widely dilated capillaries and veins as in some forms of vascular naevus. He therefore considered that the essential process was a low grade inflammation affecting primarily the capillary areas of the papillary and subpapillary regions with secondary effects in the epidermis, and that it was in no sense an angioma so that the name given to the disease was not appropriate.

Montgomery and Bailey (1935) also found severe changes in the epidermis,

mentioning moderate intracellular and intercellular oedema of the prickly layer, and varying degrees of liquefaction necrosis of the basal layer which they considered accounted for the superficial scarring which had been described clinically by some authors. They also mention endothelial proliferation in the papillary and subpapillary layers with newly formed capillaries and moderate perivascular lymphocytic infiltration in the same areas.

Thus the histological findings as described by Wise and by Montgomery and Bailey and their interpretation as showing an inflammatory process in the dermis with secondary changes in the epidermis differ markedly from the histological findings in this series and in the majority of reports from this country.

REVIEW OF THE LITERATURE.

Although it is true that angioma serpiginosum is an uncommon condition, there have been only two full papers in the literature of this country and of U.S.A. since Hutchinson's classical description in 1889 (Wise and Pollitzer, 1913; Montgomery and Bailey, 1935). There are however a number of reports of cases shown at dermatological society meetings and I have been able to study 35 of these reports in the American literature and 27 from this country. Accurate assessment of the American case reports is extremely difficult because of a wide variation in the clinical features described. This in itself may be significant when contrasted with the uniformity of the cases described in this report and, as I will show later, of many of those presented before society meetings in this country. In 18 of the 35 American case reports the diagnosis was not accepted in the subsequent discussion (Harris, 1914; Pardee, 1915; Rosen, 1919; Wertheimer, 1923; Lapuski, 1924; Feldman, 1925; Whitehouse, 1925; Blosser, 1926; Williams, 1926; Bechet, 1928; Ebert and Mrazek, 1928; O'Leary *et al.*, 1935; Robinson, 1942; Combes, 1945; Netherland and Hubler, 1945; Rattner *et al.*, 1946; Wise, 1948; Sulzberger *et al.*, 1951). In a further 8 cases the absence of discussion and the paucity of clinical details do not allow satisfactory assessment (Hyde, 1910; Engman and Mook, 1913; Ochs, 1921; Throne, 1924; Guy and Jacob, 1926; Best, 1932; Guy *et al.*, 1932; Robinson, 1941). The cases reported by Francis (1895), Traub (1932), Wise (1932), and Ringrose (1950) much more closely resembled the description given in this report. The remainder (Wallhauser, 1909; Fox, 1920; Clark, 1922; Michelson and Madden, 1937; O'Leary *et al.*, 1937; Cole and Driver, 1940) all had atypical features.

In 1913 Wise reported 3 cases, and reviewed the 22 cases reported up to that time. His 3 patients were females, and the ages at onset were 14, 20 and 28 years. The characteristic puncta as described by Hutchinson were noted in only one case and consisted only of two groups of 3 or 4 spots, despite the fact the eruption was generalized sparing only the palms, soles, face and scalp.

In the other two cases also the condition was widespread over the trunk and limbs. Areas of atrophy were noted in all 3 cases. Two of these cases were originally described by Fox (1911, 1912); one had been presented as a case of diffuse macular atrophy, and Fox noted that the appearance of the eruption on the breasts simulated that seen after x-ray therapy.

In 1935 Montgomery and Bailey reported a case of their own and reviewed the literature of the 57 cases reported up to that time. Their patient was a 66-year-old female with a more or less generalized eruption of about a year's duration. Within a further period of two months this cleared completely from the trunk and upper extremities although remaining on the legs, which a year later presented only a very faint brownish mottling. In the active stage the eruption presented as extensive pink to reddish-brown mottling, made up of groups of fine red macules and low lichenoid papules on a diffusely reddened base; there was also a fine desquamation and wrinkling over the prominent surfaces.

It is evident that both Wise and Pollitzer and Montgomery and Bailey were describing a different clinical and histological entity from that described in this paper and from the majority of the cases reported in this country in the last 50 years. These cases number 27, and of these 19 which were presented before dermatological society meetings showed a marked similarity to the cases described in this series (Hutchinson (4), 1889-92; Radcliffe-Crocker, 1894; Morris, 1896; Roberts, 1897; White, 1897; Hutchinson (Jnr.), 1907; Morris and Dore, 1912 (Whittle, 1950); Sequeira, 1912; Pernet, 1914; Gray, 1919; Graham Little, 1921; Sequeira, 1925; Parkes Weber, 1927; Barber, 1931; Goldsmith, 1939; Musso, 1953). The remaining 8 cases had atypical features or there was lack of agreement as to diagnosis in the subsequent discussion (Dockrell, 1898; Dore, 1905; Graham Little, 1915; Roxburgh, 1924; Thomson, 1936; Gray, 1931; Peters, 1937). Reference to Table II will show that 17 of these 19 cases were females, and that 16 developed the condition before the age of 16 years. It was confined to the limbs in 15 and in 5 only one leg was affected. The presence of the characteristic angiomatous puncta was stressed in most instances. There was no mention of atrophy except in Pernet's case and he was not entirely certain that definite atrophy was present. The active production of new lesions was often mentioned (Musso, Sequeira, Graham Little, Gray, Roberts, Morris and Dore). Radcliffe-Crocker, Gray and Parkes Weber all mentioned spontaneous disappearance of lesions.

DIAGNOSIS.

The criteria for diagnosis suggested by Andrews (1954) and by Ormsby and Montgomery (1954) are similar, both describing minute copper-red to bright red angiomatous puncta, the condition advancing by the formation of new

lesions at the periphery, with clearing in the centre, leaving a fine desquamation and a semblance of atrophy. A diffuse erythema may form the background in active areas. No purpura is present. Slight lichenification with incidental pigmentation may be observed. The condition affects predominately the lower extremities. It is usually slowly progressive and chronic and although involution constantly occurs, it is probably never complete. It affects both sexes at all ages. The histological criteria of these authors are similar to those described by Wise and Pollitzer and by Montgomery and Bailey.

Study of the cases described in this report suggests that it is possible to determine more exact criteria :

(i) The fundamental lesion is an angiomatous punctum varying in colour from red to deep purple. In some cases there may be a variable degree of background erythema. The degree of compressibility of the puncta is also variable but it is at the most only partial, and often the colour is unchanged by diascopic pressure.

(ii) The active production of puncta is usually gradual although long quiescent periods may occur. The resultant grouped puncta may present in serpiginous, gyrate or linear patterns.

(iii) Purpura is never present.

(iv) Spontaneous cure, partial or complete, may occur after some years. It is unlikely that atrophy occurs.

(v) It affects the female sex in most cases.

(vi) It is usually first noticed before the age of 16 years, commonly developing first in the early years of childhood.

(vii) It most commonly affects the lower limbs, being confined to one or two limbs in most cases. A widespread distribution over trunk and limbs occurs rarely.

(viii) The most frequently found histological change is a dilatation of the small capillaries of the papillary and subpapillary plexus of the dermis with or without thickening of the vessel wall ; any other epidermal or dermal change is absent or minimal.

Although sometimes a capillary angioma may show some progression after birth, it usually increases only in proportion to the normal growth of the body. Occasionally angiomatous puncta of a similar type may be found in some parts of a naevus flammeus.

There is no justification for including cases of angioma serpiginosum in the group of pigmented purpuric eruptions (Schamberg's disease ; Majocchi's disease, and the pigmented purpuric lichenoid eruption of Gougerot and Blum). However, Randall and his co-workers in 1951, in reviewing 92 cases of pigmented purpuric eruptions which had been studied at the Mayo clinic over a period of 30 years, were impressed with the close similarity between the various members of the group and included angioma serpiginosum (12 cases) with the other types.

They also comment on the striking similarity in the clinical descriptions of all four conditions, both in their own cases as well as those reported in the literature, despite the differences in diagnosis. They therefore concluded that the usual absence of symptoms, the benign nature and the obscure causative factors would seem to make their separation unwarranted. It is perhaps significant that Templeton (1927), in describing two of the early cases of Schamberg's disease reported in U.S.A. considered that it differed clinically and histologically both from Majocchi's disease and from angioma serpiginosum. He also stated that the type of angioma serpiginosum studied microscopically by Roberts differed so radically from Wise's case of angioma serpiginosum and from Schamberg's disease as to make differential diagnosis very easy.

It is likely that the grouping of angioma serpiginosum with these purpuric eruptions in the past has been mainly responsible for the differences of opinion as to the criteria necessary for diagnosis. It should therefore be recognized that angioma serpiginosum is not a purpuric eruption due to damage to vessel walls but an ectasia of existing blood vessels; this, and the characteristics mentioned above, form adequate criteria for diagnosis.

COMMENT.

Angioma serpiginosum is essentially an abnormality of the small blood vessels of the papillary and subpapillary layers of the dermis. As Roberts (1897) suggested it is not an angioma in the sense of being due to the new formation of blood capillaries but is really an ectatic condition of pre-existing capillaries, which have expanded slowly without the normal physiological brake, leading to the stagnation of blood; these permanently dilated vessels present clinically as the angiomatous puncta, which after a variable period of years may disappear spontaneously, presumably due to thrombosis. It may be that those cases which present only puncta, grouped in various patterns, are distinct from others in which there is a background of a varying degree of dusky erythema, with or without groups of small linear telangiectasies. It seems more likely however that they are all manifestations of the same process, especially as it is nearly always possible to find peripheral areas in which the typical angiomatous puncta are present, isolated or in groups, on otherwise normal skin. Red angiomatous puncta may be present in some parts of the common naevus flammeus, and the few cases in which angioma serpiginosum is reported as dating from birth or soon after may really belong to this group.

Despite our limited understanding of the abnormal process at work, it seems reasonable to accept angioma serpiginosum as a distinct clinical entity, differing in many aspects from the ordinary capillary angioma and bearing no relationship whatsoever to the group of pigmented purpuric eruptions.

Interpretation of case reports in the literature is notoriously difficult but it appears that Wise and Pollitzer, Montgomery and Bailey and certain other American clinicians have a different clinical and histological conception of angioma serpiginosum. On the other hand the general trend of interpretation of Hutchinson's original description, in the dermatological literature in this country, follows closely the cases described in this report.

SUMMARY.

Eleven cases of angioma serpiginosum are reported. The clinical and histological features and diagnosis are discussed.

The relevant literature is reviewed. The interpretation of Hutchinson's original cases in this country closely follows the series reported in this paper but differs from that accepted by American authors.

Angioma serpiginosum is a clinical entity distinct from capillary angiomas and from the group of pigmented purpuric eruptions. It is suggested that it is an ectasia of existing blood vessels in the papillary and subpapillary plexus of the dermis possibly resulting from a functional abnormality of these capillaries.

I wish to thank Dr. C. H. Whittle and the consultant staff of St. John's Hospital for Diseases of the Skin for allowing me to study these patients under their care; especially to express my gratitude to Dr. R. T. Brain and to Dr. H. Haber for their encouragement and guidance; and to thank the Institute of Dermatology for the photographs.

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INTRACTABLE PUSTULAR ERUPTIONS OF THE HANDS AND FEET.

A REVIEW OF 70 PATIENTS.

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THE purpose of this paper is to present my findings and assess the role of focal sepsis in the cause and cure of intractable pustular eruptions of the hands and feet, commonly called pustular psoriasis or pustular bacterid. I shall not include those cases which are by most dermatologists described as acrodermatitis continua with demonstrable sepsis, in which a coagulase-positive staphylococcus may be cultured from the pustule, and plays a significant if not a causative rôle. I shall also discuss very briefly the problem of treatment.

Intractable pustular eruptions of the hands and feet may present in several patterns, each having particular features of its own. One pattern has been called by Andrews (1935) a pustular bacterid, another regarded by Barber (1930) as pustular psoriasis, and a third by Audrey (1901) and by Dore (1928) as an abortive form of acrodermatitis perstans.

The essential features of the pustular bacterid type are discrete pinhead-sized lakes of pus which dry to brown macules, with scaling and erythema; the affected skin often develops a red glazed appearance. These changes are usually present symmetrically on the centre of the palms and soles and often spread to involve the entire flexor aspect of the hands and feet. The pattern described by Barber as pustular psoriasis consists of scaling psoriasiform areas in which pinhead-sized intraepidermal pustules form, and later develop into yellow spongy scabs, which, on removal, disclose a red glazed skin with innumerable flat lakes of pus. The sites of election are the eminences of the hand and inner part of the soles, often spreading on to the centre of the palms and soles. Outlying patches, separate from the original ones, may occur on the soles, palms and digits, including the skin around the nails. The features of the last and third pattern, described by Audrey and Dore as the abortive form of acrodermatitis perstans, are small solitary well circumscribed areas of pinhead-sized lakes of pus which dry to brown macules with very little surrounding inflammatory reaction, symmetrically situated on the thenar eminences and on the inner part of the soles, and are usually confined to the same areas for many years.

The most careful microscopic and cultural examinations for micro-organisms

in the pustules in all these cases are almost invariably negative ; occasionally a staphylococcus is grown but is probably of no significance. All these eruptions are probably of the same fundamental significance and represent an individual pattern of reaction to some stimulus. This pattern of reaction is possibly a combination of psoriasis with an ordinary catarrhal eczematization. It is a constitutional reaction like eczema, dependent upon the individual and not on the exciting cause. Of the 70 patients under review, 4 had typical lesions of eczema and 13 had psoriasis from time to time on other parts of the body. This reaction like other constitutional reactions may be excited or influenced by a variety of factors, such as acute or chronic infection, hormonal or emotional stress. Both Barber and Andrews believed that focal sepsis, particularly involving the teeth and tonsils, was an important exciting cause, and that its removal produced a permanent cure. Ingram (1954) recently has stated that about 30% of his patients with pustular psoriasis of the hands and feet had some septic focus, and that in these treatment of the sepsis rarely produced a permanent cure.

MATERIAL AND CONCLUSIONS.

Most of the 70 patients have been examined by me, and many have been attending the skin department for several years. Twenty-three (33%) were found to have a septic focus ; 14 had one or more apical dental abscesses ; 7 had chronic tonsillar infections and 2 had chronic otitis media. Eighteen had their focal sepsis removed. In 2 cases the eruption cleared within 6 months and it has remained clear for 2 years. In the remaining 16 patients the eruption has remained active for 2-14 years, although 6 have improved considerably. Some of these patients improved temporarily, and some even cleared after removal of the focal sepsis, but usually, within a few months, they relapsed. Of the remaining 5 patients, in whom focal sepsis was not removed, 3 had cleared and remained clear for 6 years or longer, and in 2 the lesions are still active after 1 and 2 years respectively.

No focal sepsis was found in 47 patients. In 4 of these the eruption has cleared after lasting from 1-6 years, and they have remained clear for periods of 6 months, 2 years, 3 years and 5 years respectively. In the remaining 43 patients, the disease was still active, although 12 have improved. The eruption has been present for 2-4 years in 19, 5-9 years in 17, and 10 years or more in 4.

The relative proportion of patients cured and of patients who still have active disease is the same in the group with focal sepsis as in the group in which no focus was found. This suggests that the removal of focal sepsis in these patients plays little or no part in producing a permanent cure, and improvement is probably spontaneous. This conclusion is supported by the fact that 3 patients in whom a recognized focus of sepsis was not removed

also recovered. In a few patients an acute infection preceded the onset or an exacerbation of the skin lesion. The eruption may persist for many years with periods of exacerbation and remissions. The duration was 30 years in one patient, and a remission lasted 5 years in another before the recurrence of a further active phase.

In this respect I should like briefly to mention a patient I have recently seen. A woman aged 45 developed a pustular eruption about the nail fold and nail bed of the left great toe 7 years ago and acrodermatitis continua was diagnosed. Two years later the eruption cleared after permanent destruction of the nail matrix. For the last 2 years a persistent pustular bacterid type of eruption of the sole of the same foot has developed.

The natural history of these cases may be illustrated by the following patients. The first is a man who developed pustular lesions about the tip of the left thumb just before he entered the Royal Navy at the age of 15. During the next 3 years he remained more or less free of trouble. After his discharge from the Navy, the lesions began to relapse and when he was seen for the first time one year later he had a typical eruption of the pustular psoriasis pattern on the thenar eminences, palms and wrists, and also on the tips of some of the digits. At this time he was found to have infected tonsils and these were later removed. Within a few weeks of their removal the eruption cleared for 6 months but then he relapsed again. The lesions have persisted with remissions and exacerbations for the last 3 years, at times temporarily improving with local treatment. On one occasion a relapse followed an acute attack of influenza.

Another patient aged 34 developed a pustular bacterid type of eruption on the left sole. During the next 2 years the patient became aware that exacerbation repeatedly coincided with activation of a chronic apical dental abscess. At the end of 2 years the dead tooth was extracted and the apical abscess which had tracked into the maxillary antrum was drained. This was not followed by any improvement in the skin. For the last 3 years the eruption has persisted with episodes of exacerbation and remission. The lesions have remained confined to the sole and the inner aspect of the foot, in spite of little or no treatment except for a 6-weeks' course of sulphonamide which failed to influence the eruption.

The course of these eruptions resembles that of dermatitis herpetiformis in many respects, tending to resolve spontaneously after many years of exacerbations and remissions. It is of interest in this respect to recall Dr. Hellier's case (1956) of a man aged 55 with a pustular bacterid type of lesion of the hands and feet of 10 years' duration. During one of the active phases, a widespread pustular vesicular eruption developed, which resembled the pattern of dermatitis herpetiformis so much that that diagnosis was seriously considered. The eruption on the hands and feet was controlled by dapsone therapy.

Both Barber and Andrews thought that the removal of focal sepsis was followed by a cure in most patients. It is, however, necessary to have a long-term follow-up to be certain that the cure is permanent, and I do not think that the removal of focal sepsis in these patients does produce a permanent cure. Acute sepsis or an acute illness may provoke or activate these intractable pustular eruptions of the hands and feet, but the same is true of most other reactions, including psoriasis.

TREATMENT.

These patients are difficult to treat apart from attention to focal sepsis. Chemotherapy and the administration of antibiotics have not often affected the course of the disease permanently, although the general and local use of such measures upon occasion produces temporary improvement. Steroid hormonal therapy similarly has not helped. Most patients are in good general health, and at times most of them benefit from some form of local treatment. Here tar seems to be the most helpful, either as the crude product or in a paste or liquor picis carbonis as a paint or wet dressing. Sometimes ichthammol paste alone or following tar treatment gives relief.

SUMMARY.

Intractable pustular eruptions of the hands and feet present as several patterns called pustular bacterid, pustular psoriasis and an abortive form of acrodermatitis perstans. These are probably all of the same fundamental significance and represent an individual pattern of reaction, probably a combination of psoriasis with an ordinary catarrhal eczematization.

A review of 70 patients was undertaken to assess the role of focal sepsis in the course and cure of pustular lesions of hands and feet.

Removal of focal sepsis in these patients probably plays little or no part in producing a permanent cure, and improvement is spontaneous after many years of remissions and exacerbations.

Treatment is briefly discussed.

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GENERALIZED COMMON AND HYPERTROPHIC WARTS.

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COMMON warts may be profusely disseminated and may then become confluent hypertrophic and atypical lesions. Descriptions of this type are to be found in the monograph by Freudenthal and Spitzer (1933); the more recent literature includes the report by Costa (1946) on unusually extensive common warts and confluent condylomata acuminata, and the communication by Hermans and Nater (1956) on disseminated familial common warts and condylomata acuminata. Costa's case, of a Brazilian 30 years old, greatly resembles our own; his patient suffered for 15 years from confluent lesions involving the dorsa of feet and hands, and some other areas.

CASE REPORT.

CASE 1.—The patient, a labourer 23 years old, was admitted to hospital complaining of extensive wart-like lesions of 5 years' duration. The lesions developed suddenly, without any apparent cause, first on the dorsum of the left foot and spread rapidly over the lower and upper extremities.

His parents were not related. No other member of the family had warts. The patient was treated locally with silver nitrate but without success, and the lesions spread gradually to new regions.

Skin changes were scattered chiefly on the upper and lower extremities with occasional lesions on the face and trunk. Mainly the distal parts of the extremities were affected, particularly the feet and hands.

The primary lesion was a superficial papule variably hypertrophied and hyperkeratotic. The more recent lesions were either round or polygonal, several millimetres in diameter, flat and only slightly hyperkeratotic. Older lesions were larger, hypertrophic with fairly distinct hyperkeratosis, and very much resembled typical common warts. Some became confluent forming extensive hyperkeratotic and papillomatous plaques. Occasionally the papules were arranged along lines of scratches.

Lesions on the hands and feet were much more numerous on the dorsal than on the flexor surfaces. On the dorsum of the left foot there was a confluent lesion extending to the leg and formed by the merging of separate wart-like lesions which were still visible on the periphery. The surface was hypertrophic, papillomatous and hyperkeratotic (Fig. 1). Distally the changes extended to the toe-nails, involved the nail folds and caused subungual hyperkeratosis with elevation of the nail plates. They extended also to the interdigital spaces, causing considerable maceration. In the proximal part of the lesion there were still visible single papules, partly in groups, partly confluent. The smaller ones still retained the morphological features of warts whereas others, distinctly hypertrophic and confluent, resembled papillomas. On the soles the papules were more deeply situated with a tendency to merge and had a reticular arrangement; hyperkeratosis was less pronounced. They were here similar to mosaic warts.

The warts showed a distinct tendency to affect periungual and subungual areas. The nail folds were affected on some fingers only but almost all fingers showed

pronounced subungual hyperkeratosis with partial exfoliation or destruction of the nail plates. These lesions had the typical features of periungual common warts. The periungual warts on the right foot were similar in appearance but the left foot differed owing to the confluent character of the lesion and had the features already described.

On the proximal parts of the limbs there were merely single scattered warts, and on the face occasional flat small ones, about the colour of normal skin.

Mucous membranes were normal. Lymph nodes were not enlarged.

Histology.—Biopsies were made of morphologically different lesions from various sites. Four were of the type of common warts (from the dorsum of the hand, palm and sole) and had a similar histological structure; two specimens taken from the confluent papillomatous lesion were identical.

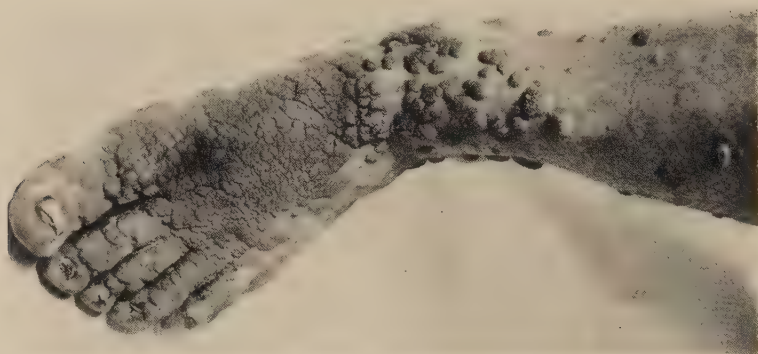


FIG. 1.

The specimen taken from the lesion resembling a common wart had the typical histology of that condition. There was a distinct hypertrophy of the epidermis, involving the horny layer, which had a loose basket-like arrangement of keratin, and the granular and prickle-cell layers (Fig. 2). Rete pegs were moderately hypertrophied, elongated and widened. The granular layer and the upper rows of prickle-cells were slightly vacuolated, but not to the degree found in epidermodysplasia verruciformis. Inclusion bodies were absent. There were no changes in the basal-cell layer. In the dermis there were slight round-cell infiltrations around the superficial vessels.

The specimen from the foot showed very pronounced confluent hyperkeratosis, a uniform hypertrophy of the granular and prickle-cell layers, and considerable elongation of rete pegs. There were minimal inflammatory infiltrations around the capillary vessels.

The specimen from the papillomatous lesion showed very pronounced hypertrophy of the entire epidermis, hyperkeratosis, granulosis, acanthosis and papillomatosis (Fig. 3). In some places there were foci of parakeratosis of the type found in warts. The picture was here identical with that seen in old warts. Neither vacuolation nor inclusion bodies were seen.

General examination.—No abnormalities were revealed. There was a small corneal infiltration resulting from an earlier keratitis of unknown origin.

Inoculation of 3 adults with material from verrucous lesions was unsuccessful.

Treatment.—For general treatment Liq. arsenicalis was administered over a period of 6 weeks; then chloramphenicol in a total dose of 26.0 g. and Largactil

(100 mg. daily over 8 weeks) without any improvement. We applied also locally an ointment of 0.1% colchicine without success. The only successful treatment was curettage of lesions, freezing with CO₂ and x-ray irradiation.

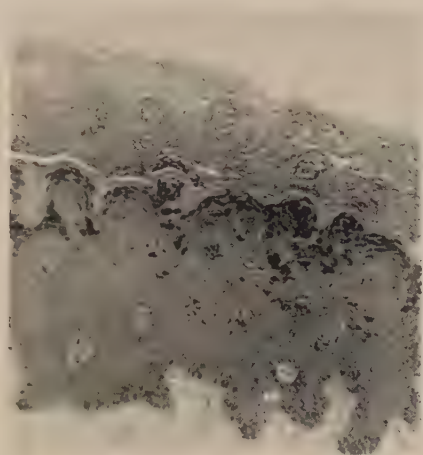


FIG. 2.

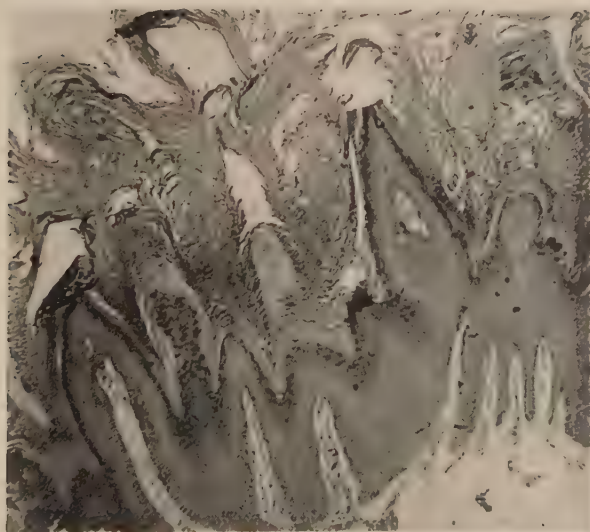


FIG. 3.

The periungual lesions were irradiated 5 times in doses of 500 r by the Chaoul method (kV. 50, filter 2.5 mm. Al.) at 7-10 day intervals; the dorsa of the hands were irradiated 4 times in identical doses (Dr. S. Zakrzewski). In some areas there was a transient Roentgen reaction which left no traces.

On the left index a wart reappeared at the irradiation site and was removed with the electrocautery.

The confluent lesion on the left leg was curetted bit by bit and frozen with CO₂ snow, and after prolonged treatment the majority of the changes disappeared.

The lesions on palms and soles were also curetted and frozen with CO₂. These procedures, repeated many times and followed by a pronounced and sometimes prolonged inflammatory reaction, were very trying for the patient.

During the treatment new lesions appeared scattered irregularly over the extremities and also on the face, occasionally clearly along scratches. It was apparent that the patient inoculated himself with his hands from subungual and periungual warts, and after the periungual lesions had disappeared no new warts developed. The treatment was not finished and the patient was discharged at his own request after notable improvement; however, there were still quite numerous discrete and grouped wart-like lesions left.

DISCUSSION.

The case described has all the features of generalized, confluent and hypertrophic warts, i.e., primary lesions of the common wart type, and a typical histological structure—hyperkeratosis, granulosis, acanthosis, papillomatosis and a limited degree of vacuolation in occasional smaller lesions (absence of inclusion bodies does not contradict the diagnosis (Lipschütz, 1924; Blank *et al.*, 1951; Lyell and Miles, 1951))—the presence of lesions along scratches (spontaneous auto-inoculation), and the partly favourable results of local treatments usually applied in cases of warts. A peculiar characteristic of this case was the unusually large area covered and the tendency to form verrucous confluent lesions. However, these features are not of basic importance and are of a merely quantitative character.

The case has to be included in the generalized form of common and partly hypertrophic warts (verruccosis generalisata).

The greatest difficulty in diagnosis consists in that the verrucous type of reaction is not entirely specific and that identical changes may occur in various diseases. For instance, in Darier's disease, there may appear on the dorsa of hands lesions indistinguishable from warts (mostly flat ones), but differentiation is easy on the histological picture. In acanthosis nigricans there are occasionally single disseminated lesions strictly resembling warts, but diagnosis is determined in these cases by the other typical lesions and by the different histological picture. Verrucous lesions may occur also in acrokeratosis verruciformis (Hopf) and in verrucous naevi; we disregard here epidermodysplasia verruciformis (Lewandowsky and Lutz), where the changes bear the character of disseminated flat warts, and only single papules resemble common warts.

In order to illustrate the difficulty in differential diagnosis we may quote a case of a peculiar type of naevus or atypical form of acrokeratosis verruciformis in which the skin changes had the features of common warts.

CASE REPORT.

CASE 2.—A labourer 23 years old attended the Clinic complaining of changes on the hand and forearm which developed a year before. At first there were single

verrucous lesions diagnosed as warts and treated with x-rays (total 1500 r) without success. The lesions spread slowly but continuously, and the old ones merged to form elevated verrucous and hyperkeratotic areas. There were no subjective symptoms.

The parents of the patient were not related and there was no skin disease in the family.

General examination showed no abnormality.

Skin changes involved the lateral edge of the left hand and the lateral edge of the left index, extending from the nail-fold up the distal third of the forearm in a more or less linear arrangement. The primary lesions were round papules a few millimetres to 1.5 cm. in diameter, hard, with a very pronounced hyperkeratosis of the surface. The verrucous lesions had a tendency towards grouping, forming confluent areas of irregular shape and hypertrophied hyperkeratotic surface (Fig. 4). The lesions involved the nail fold and extended partly on to the nail bed, but without causing destruction of the nail plate.

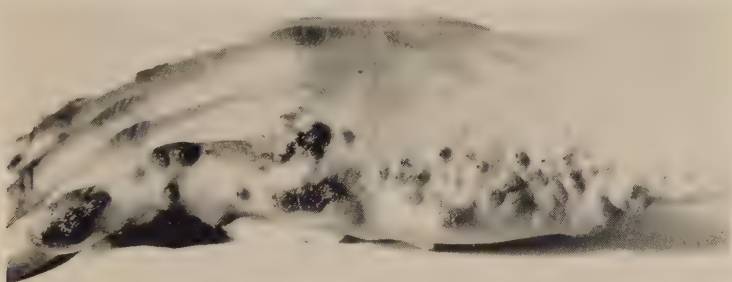


FIG. 4.

Histology.—There was pronounced hypertrophy of the entire epidermis, affecting particularly the horny layer which was generally compact and contained no residual nuclei (Fig. 5). The granular and prickle-cell layers showed no vacuolation. Rete pegs were elongated, reaching deep into the dermis. In the papillary layer there was minimal infiltration of lymphocytes and histiocytes around the small vessels.

Course and treatment.—After removal of the horny deposits with a keratolytic ointment the lesions were partly electrocoagulated, partly frozen with CO₂ or curetted. The treatment was carried out by stages in the out-patient department and generally it was unsuccessful; improvement was only partial and temporary.

This case does not fit with the diagnosis of warts since the lesions were limited to the dorsum of one hand and forearm and had a distinctly linear arrangement. The histological picture is also of essential importance: in warts, in addition to hyperkeratosis, granulosis, acanthosis and papillomatosis there are also a specific kind of parakeratosis with variable vacuolation of the cells of the granular and prickle-cell layers and, occasionally, also inclusion bodies. In Case 2, unlike Case 1, the histological changes consisted in a uniform hypertrophy of all epithelial layers, the horny one in particular, and this occurs in the acrokeratosis of Hopf and epithelial naevi.

On evidence of the clinical and histological pictures Case 2 might be diagnosed as acrokeratosis verruciformis (Hopf) although it is not typical. That disorder, according to Hopf, is a developmental abnormality of the keratoma type (Hopf, 1931 ; 1933), and according to some other authors is an abortive form of ichthyosis with a tendency towards limited hyperkeratosis (Klücken, 1952). The verrucous lesions develop immediately after birth, in early childhood or at the age of puberty ; they are symmetrical and morphologically intermediate between flat and common warts. Occasionally there is a concomitant slight palmar and plantar keratosis which Hopf believes to indicate a relation with keratoma.

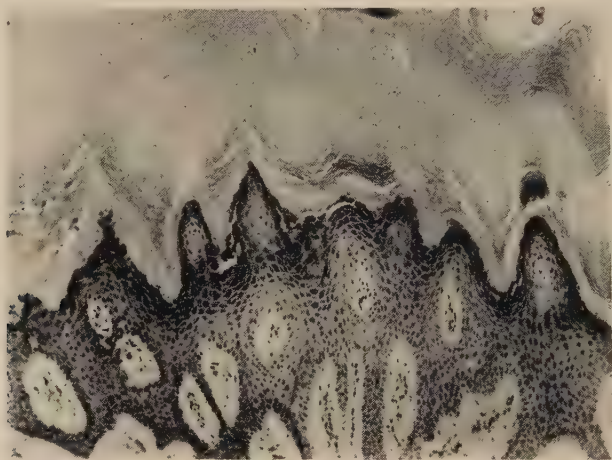


FIG. 5.

In Case 2 the changes set in as late as in the twenty-second year of life, they spread consistently though slowly, they were more elevated and hyperkeratotic than in typical cases of acrokeratosis verruciformis and, moreover, they were unilateral.

The linear and unilateral arrangement clearly suggests a naevus. Consequently, the condition might have been diagnosed as a unilateral late epithelial naevus whose peculiarity consisted in that it was composed of single or confluent warts, and that it appeared at the twenty-second year of life and had some tendency to spread. The histological picture is compatible with this as well as with acrokeratosis (Hopf). Acrokeratosis verruciformis is indeed probably a variety of hard naevus, in which the primary lesions are of the wart type and involve only the extremities. If this is so, it appears unnecessary to distinguish between the verrucous naevus and acrokeratosis verruciformis.

In general, it ought to be said that diagnosis of warts is not always easy since common warts may present an unusual clinical picture with many atypical

morphological features and, on the other hand, warty lesions may occur in the course of various other diseases.

It may happen, as it did in both our cases, that the clinical character of the skin changes by itself does not permit a firm diagnosis. Histological examination is then highly important.

In the differential diagnosis of warts and wart-like lesions of different aetiology it is not infrequently helpful to observe the course of the disease. A valuable clue is occasionally gained when new lesions arise from spontaneous auto-inoculation.

As demonstrated by our cases, neither late occurrence of the disease nor the spreading of lesions are relevant in distinguishing between warts and wart-like changes of the naevus type.

Unusually prolonged persistence and resistance to treatment of generalized common and hypertrophic warts probably depends upon certain still unexplored individual peculiarities, and this applies also to generalised flat warts occurring in the clinical form of epidermodysplasia verruciformis (Lutz, 1946 ; Miescher, 1948 ; Hermann, 1954). These individual peculiarities are also likely to account for the tendency to develop confluent hypertrophic lesions differing very notably from known morphological types of either warts or condylomata acuminata.

SUMMARY.

The authors describe a case of generalized, persistent and markedly treatment-resistant common and hypertrophic warts of an unusual clinical type. The histological picture of early lesions showed the typical features of warts while within confluent lesions there were changes of the type found in papillomas.

The authors discuss the differential diagnosis of atypical warts and wart-like lesions of different aetiology, particularly those of the type of verrucous naevi, or acrokeratosis verruciformis (Hopf.). Histological examination is very helpful and reveals, even in entirely atypical warts, in early lesions, parakeratosis and vacuolation of epidermal cells.

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THE EFFECT OF LOCAL APPLICATION OF HYDROCORTISONE IN DERMATITIS HERPETIFORMIS.

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LOCAL therapy is remarkably ineffective in dermatitis herpetiformis, and systemic treatment is the recognized method of controlling the symptoms and eruption. This is not surprising when it is considered that the disease is almost certainly the result of some, as yet unknown, systemic abnormality. It is of interest, therefore, to observe the effect of local application of hydrocortisone in this disorder.

TABLE I.

Case No.	Hydrocortisone ointment.*				Control ointment.			
	State before treatment.	Duration of application (weeks).	Effects.†		State before treatment.	Duration of application (weeks).	Effects.	
			Relief of itching.	Inhibition of lesions.			Relief of itching.	Inhibition of lesions.
1	Clear	2	++ several hours	0 relapsed	Slight activity	2	0	0 relapsed
2	Active	7	+++	+++	..	..	..	..
3	"	16	+	0	Slight activity	3	0	0
4	Clear	2	++ 1-2 hrs.	0 relapsed	..	..	..	..
5	"	1½	± ½-hr.	0 relapsed	..	..	..	..
6	"	1 (1%)	0	0 relapsed	Clear	1	0	0 relapsed
7	Slight activity	30	+++	+++	..	..	..	..
8	Active	2	0	0	Slight activity	4	0	0 worse
9	"	4	+++	+	Active	2	0	0
10	Slight activity	26	+++	+	Clear	1	0	0 relapsed
11	Active	10	+	0	..	..	..	..
12	"	1 (1%)	0	0	..	..	..	..
13	"	1	+	0	Clear	1	0	0 relapsed
			15-20 min.					
		3	++	+	..	..	..	..
		9	+++	+++	..	..	..	..

* 2½% hydrocortisone ointment used unless otherwise stated.

† +++ complete; ++ considerable; + slight; 0 none.

Thirteen patients were chosen for trial. The preparation used was hydrocortisone acetate in a greasy base; 2½% ointment was mostly used but in some cases the effect of 1% ointment was also observed. Control ointment consisting of the base only was used in 8 of the cases. Any means of identifying the preparation was removed so that patients received unlabelled tubes of ointment with instructions to use 2-4 times daily. Substitution of control for active

ointment and *vice versa* was made without the patient's knowledge. Eleven of the patients, prior to the trial, were under control with dapsone, and this was withdrawn before treatment with hydrocortisone was started. In some cases, where the local treatment failed to give relief, the subsequent irritation was so intense that the patients were forced to resume dapsone.

Results are shown in Table I. Patient 12 had had no previous treatment and was later completely controlled with dapsone. Patient 13, a child, did not respond at all to dapsone and was given fairly large doses of liquor arsenicalis for several months without any benefit. Cases 2 and 6 showed complete relief whilst using ointment: case 13 showed complete relief but was also taking liq. arsenicalis in diminishing doses while the ointment was applied. The remainder showed partial relief which took the form of alleviation of irritation for periods varying from 15 minutes to several hours after each application. In none of these cases, however, was the effect sufficient either to abolish visible skin lesions or to prevent further lesions occurring.

COMMENT.

The series of cases is small, but certain conclusions can be drawn from this trial. Comparison with the effects of control ointment show that local application of hydrocortisone does have some beneficial effect. The effect is only a temporary one but all the patients who benefited were quite emphatic that the decrease in itching occurred within a few minutes of the application. This effect was repeated with each application.

Three patients with severe itching were unable to do without dapsone for more than a few days. All these, however, noticed that on resumption of dapsone as well as hydrocortisone ointment they were able to achieve complete control of the disease with a lower dose than had previously been required. This is an important point. It may be found that cases which are difficult to control with either sulphapyridine or dapsone may be brought under control more easily if hydrocortisone ointment is applied simultaneously. Furthermore, it may be desirable in certain circumstances, for example during pregnancy, to reduce the dose of the drug as much as possible and again the concomitant use of hydrocortisone ointment may be of value. It may also prove to be of assistance in controlling the lesions of juvenile dermatitis herpetiformis. It is well known that large dosage of liq. arsenicalis is the most effective treatment in that condition, and any remedy which will allow smaller doses to be equally effective is valuable.

It appears, therefore, that although local hydrocortisone therapy is by no means completely effective in controlling the symptoms and eruption of dermatitis herpetiformis, it yet has a useful place in the treatment of some cases.

I wish to acknowledge my indebtedness to Messrs. Upjohn for kindly supplying the hydrocortisone ointment (Cortef) and control ointment; and to Dr. G. Harvey for permission to publish these cases.

A CASE OF RECURRENT HERPES ZOSTER.

J. LEURER, M.D. (Zürich).

Department of Internal Medicine, Shaarei Zedek General Hospital, Jerusalem.

HERPES ZOSTER recurrences are rather rare (Grundmann, 1933 ; Hruszek, 1934). Although various cases have been reported, most text-books and reviews do not mention the possibility of recurrence.

The following case of recurrent herpes zoster was connected with three other zoster cases in the same family.

CASE REPORT.

In August 1954 a 70-year-old woman was admitted to our department with typical herpes zoster of the 5th left dorsal segment. She was treated with intravenous sodium iodide without much benefit.

In October 1956 the patient returned to us with a new zoster eruption.

The patient had contracted varicella as a little girl. In 1939 she had suffered from pyelitis, and some years ago a raised blood pressure had been noted. All her life she had been anaemic. About four months prior to her second hospital admission she had been treated with traction and heat for cervical spondylosis.

Examination in 1956 revealed herpes zoster at the 10th left dorsal segment, stopping sharply at the midline on the abdomen, but crossing the midline for about 2 cm. on the back. At a level corresponding to D-5 (left, the site of her first eruption) a number of white hypoaesthetic spots (2×2 to 4×10 mm. in diameter) could be seen.

Temperature and pulse were normal, and blood pressure ranged from 155/70 to 205/105 mm. Hg.

Laboratory examinations showed moderate anaemia, serum globulins were slightly raised, Weltmann was 8. All other routine tests were normal ; Kahn reaction was negative ; skiagram of the spine revealed spondylosis, most marked at the dorsal part.

The patient did not suffer from excessive pain and no specific treatment was attempted.

Between the two hospital admissions of our patient, three members of her household fell ill with herpes zoster : In January 1955 a 7-year-old boy—at L1-2 ; in June 1955 an 89-year-old man—in the auricularis magnus region ; and in September 1955 a 56-year-old woman—at D 3-4.

DISCUSSION.

Since an attack of herpes zoster usually confers immunity, there must be some special factor in recurring cases. Two explanations have been offered :

- (a) Different strains of virus are involved in these cases (Hiller, 1949) ;
- (b) patients with recurring zoster lack immune bodies (Stern, 1920).

The second explanation may perhaps be enlarged in scope, to include cases with zoster-predisposing, or zoster-sensitizing, factors (e.g. mechanical nerve

injuries, some intoxications—Stern)—so-called “symptomatic” zoster. Patients with such factors might suffer from a zoster recurrence at times when their immunity is overcome by these factors plus virus. Two clinical observations are in accordance with this assumption: Hruszek, writing on the rarity of zoster recurrences, added that “arsenical herpes is not infrequently recurrent”, and Little (1937) also noted that “traumatic (zoster) cases may show frequent recurrence”.

Herpes zoster is known to be slightly contagious and to cause small epidemics (Stern; Ebert, 1949). Such epidemics tend to occur in short outbreaks, the intervals between individual cases varying from a few days only (Bacmeister, 1920; Fuhlrott, 1920; Dahl, 1949) to one month (Pudar, 1948). The family reported here shows a somewhat different epidemiological pattern, the patients being affected at intervals of 3, 5 and 6 months one from the other, while our own patient had her recurrence about a year after the last of the other cases. Perhaps these facts are best explained by assuming that our patient acted as a virus carrier, now and then infecting susceptible individuals, and that when her resistance to the virus was lowered, due perhaps to the (zoster-sensitizing?) traction treatment a short time before, she suffered from a recurrence.

SUMMARY.

The case of a patient with recurring herpes zoster, who infected three other people, is reported.

It is assumed that zoster recurrences are caused by the synergistic action of virus and zoster-predisposing factors, lowering tissue resistance so as to overcome immunity.

Owing to the unusual form of the reported family outbreak, it is thought that the primary case acted as virus carrier.

I am indebted to Dr. K. Horvat, the patient's family practitioner, for supplying me with details of the other three cases; to Dr. M. Michael for his suggestions, and to Dr. E. Gidron for help and advice.

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BOOK REVIEW.

SEQUEIRA.*

SEQUEIRA was a great teacher, and his two distinguished pupils carry on his traditions of soundness in the essentials and awareness of recent advances. Like "H. W. B.", who reviewed the fifth edition in 1947, the present reviewer is frankly amazed at the completeness with which the subject is covered—the rare hyalinosi cutis seems to be the only recognized entity which fails to find mention.

Dermatological classification has always been a problem, and to raise objections to the authors' scheme is to run the grave risk of being challenged to propound a better. Where in this work a dermatosis appears in what might seem to be queer company, e.g., pityriasis rosea among the seborrhoeides, a reason is usually given. Tropical diseases receive a good share of attention, including a lucid account of leprosy by Cochrane; this feature will appeal to readers not only overseas, but also in Britain, where exotic diseases are much less uncommon than they used to be.

The style is easy and fluent and the discussions are clear and logical, but a somewhat freer use of the humble, but sometimes necessary comma, would be an improvement. Misprints are rather too common; many of the Latin and Greek derivations are mis-spelt. In at least two places the meaning is obviously the opposite of what is written—on page 250 "parasitic diseases are eliminated by the finding of the parasite" and on page 760 the seborrhoeides are said to "depend upon an adequate supply of vitamin B and a balanced diet". One notes with approval the statement that there is growing interest in x-rays generated by kilovoltages up to 50, but it is surprising that no mention is made of Chaoul or contact therapy, which in the opinion of many is the method of choice in rodent ulcer, early epithelioma, molluscum sebaceum and plantar wart. The bare statement on page 606 that *Treponema pallidum* was discovered by Schaudinn in 1905 does less than justice to the equal and essential part played by E. Hoffmann in what was a very close collaboration.†

The numerous illustrations are for the most part excellent, although one or two of the coloured plates are reminiscent of the nineteenth century. This is, in fine, a first-class book, which the practitioner will discover to be a veritable mine of accurate and very practical information, and its authors are to be heartily congratulated on it.

J. F. S.

* *Sequeira's Diseases of the Skin*. Sixth Edition. 1957. London. J. & A. Churchill Ltd. JOHN T. INGRAM, M.D.(Lond.), F.R.C.P.(Lond.), and REGINALD T. BRAIN, M.D.(Lond.), F.R.C.P.(Lond.). 843 pages, 426 illustrations. Price £5 5s.

† For an authentic account of this exciting episode in dermatological history, see Memmesheimer and Armuzzi (1955) *Derm. Wschr.*, **131**, 12, 289.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President.—Dr. L. FORMAN.

18 October 1956.

Bullous Urticaria Pigmentosa.—Dr. N. A. THORNE.

This boy, aged two months, was born ten days prematurely, weighing 7 lb. 5¼ oz. His parents were healthy and there was no consanguinity. His mother suffered from an attack of jaundice one month before he was conceived but her gestation period was without complication. He has a brother, aged five, who is alive and well.

At birth the baby was healthy, apart from the skin which was covered with papular and nodular lesions varying in colour from yellow to brown. There were also a number of vesicles. The child has remained healthy but further vesicular and occasional bullous lesions have appeared. The eruption seems to be free from irritation. Urtication can be produced by gentle rubbing. Investigation showed 83% haemoglobin, W.B.C. 14,900 (polymorphs 60%, lymphocytes 40%), serum cholesterol 250 mg./100 ml., blood W.R. negative. A biopsy from one of the nodular lesions showed the presence of focal dermal infiltration with mast cells when stained with toluidine blue. The diagnosis of bullous urticaria pigmentosa seems to be satisfactorily established, in view of the skin lesions, the presence of urtication and the demonstration of mast cells histologically. *Incontinentia pigmenti* was considered but there is no eosinophilia, which was stressed by Epstein *et al.* (1952) as being present in the bullous phase of this disease.

Only 28 cases of this condition appear to have been described in the literature. The first case was described by Nettleship (1869). Of the 16 cases reviewed by Dewar and Milne (1955) only two showed lesions at birth. In four, the lesions appeared within the first 2 weeks of life and in eight cases between the ages of 2 weeks and 4 months. The remaining two appeared at 16 months and in adult life respectively. They considered that bullous urticaria pigmentosa was probably a systemic disease with an abnormal increase in mast cells in many tissues and organs.

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Nodular Dyselastosis with Cysts and Comedones.—Dr. J. H. ALLISON (for Dr. RAY BETTLEY).

A man aged 68 first noticed swellings and blackheads around his eyes about 4 years ago. Fresh lesions have continued to appear.

Examination.—Many small nodules and comedones in the periorbital skin, which shows yellowish areas of elastic degeneration.

Histology.—Cystic dilatation of the hair follicles with diminution of the elastic fibres.

Comment.—This case appears to fit the description of Favre and Racouchot (1951). They describe four cases occurring in men over the age of 50, and remark on the superficial clinical resemblance to colloid milium.

DISCUSSION.

Dr. BRIAN RUSSELL: The lesions in this case are probably related to his past work with tarred nets.

Dr. G. B. DOWLING: These lesions are not infrequently seen in elderly men and may be a manifestation of ageing. Is this not a common form of senile degeneration of the skin which may be associated with cutis rhomboidalis of the neck and with giant comedones in or about the inner concha?

REFERENCE.

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Incontinentia Pigmenti.—Dr. G. A. BECK.

B. P—, girl aged two weeks.

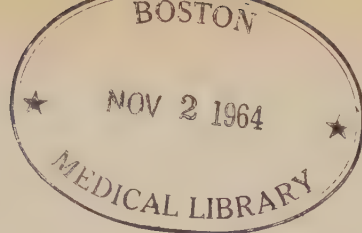
Family history.—Third child of an English father and Swiss mother. The second child is a boy with typical atopic eczema who is now reported to have asthma as well. His mother had eczema as a baby but was healthy during her pregnancy and delivery was normal.

History.—When 2 days old, he developed an eruption on the arms and buttocks which subsequently spread to the scalp, trunk and all four limbs. Initially it resembled a red burn in streaks, subsequently developing "blisters". These appeared to contain water but did not exude on rupture. The lesions on the upper extremities are already fading and beginning to scale and some of them show considerable wartiness.

Examination.—More or less bright red papules of irregular shape tending to form lines, on the back of the legs and thighs. Some are surmounted by yellow crusts, particularly on the scalp where the skin is largely obscured by patches of rather yellow opaque crusts.

I first saw this child 2 days ago and I thought it of interest to see the lesions in the early bullous stage. Even now the lesions on the arms are beginning to show the hyperkeratosis characteristic of the second phase of this eruption.

On looking up the records, I was surprised to find how frequently this abnormality is associated with other congenital defects. The latter occurred in more than 50% of cases in some series. Such defects vary over a wide range and many of them are grave, such as mental defect and hemiplegia. There is so far no clinical evidence of any associated abnormalities in this case.



NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Liverpool, October 1956.

Traumatic Calcinosis.—Dr. D. G. FRESHWATER.

A man, aged 38.

This patient burnt the back of his left calf and ankle with molten sodium in July 1955. The burns were treated with penicillin tulle gras at the time, and later the slough was excised. There was delay in healing and a skin graft was performed in August 1955 which healed completely.

In December 1955 folliculitis appeared and in February 1956 traumatic calcinosis was first diagnosed. There was at that time a low grade impetigo with infective dermatitis and follicular lesions, from which could be extruded brittle bodies which on analysis were shown to be composed of calcium salts. The traumatic calcinosis appeared over the anterior surfaces of the leg and ankle and not over the area which had first been injured.

Investigations (February, 1956).—Serum sodium 320 mg.%, serum potassium 16 mg.%, serum calcium 10 mg.%, inorganic phosphate 2 mg.%, alk. phosphatase 6 units per 100 ml.

He has been treated with occlusive dressings of Ichthopaste and Elastoplast bandages and has made good progress.

Extramammary Paget's Disease.—Dr. C. MCGIBBON.

A man aged 64, a checker, first presented himself with perianal irritation in February 1956. The internatal cleft was red and excoriated, and as the rash and the irritation had commenced twelve months before, in association with an appendix abscess, it was at first thought that the condition might be tuberculous. This proved to be not so and as the excoriated area was extending with exuberant granulations, a biopsy was performed. The clinical suspicion of extra-mammary Paget's disease was confirmed. Two subsequent biopsies confirmed this. Sigmoidoscopy was normal.

While under observation, the reddened velvety area in the internatal cleft has doubled its size and become surrounded by a raised area of skin which has spread progressively on to the buttocks and presents a sharply circumscribed erysipeloid edge. Also during this latter period of increased activity, the right inguinal gland became enlarged. Biopsy shows the secondary deposits of squamous carcinoma.

TRANSVAAL DERMATOLOGICAL SOCIETY.

Cases shown during 1956.

Foreign Body Granuloma.—Dr. M. CHITTERS.

White male, aged 44 years. Painless hard papules had arisen in the previous four months over the dorsa of the fingers, with isolated lesions on one palm and near one elbow. Twenty-three years before he had been peppered with quartz-like material in an explosion of the ventilation system underground in a goldmine.

On examination the papules were about $\frac{1}{3}$ in. in diameter.

Histologically the lesions showed a sarcoid structure with crystalline foreign bodies in the giant cells. These crystals were not identified. Micro-incineration was negative for silica.

Chest x-ray showed no sarcoidosis nor any other abnormality.

Comment.—The long latent period between the accident and the onset of the reaction is remarkable.

Melkersson-Rosenthal Syndrome: Response to Prednisone (Meticorten).

—Dr. L. J. A. LOWENTHAL.

White male, aged 73 years. Following a keratitis of the right eye of unknown cause 16 months before, the patient gradually developed unsightly swelling of the lips and enlargement of the tongue. The inner surfaces of the cheeks became rough and the tongue developed an adherent white membrane with small growths that sometimes bled on injury. There was dribbling and epiphora. Seven years previously he had had a "stroke" affecting one hand and both legs, from which he recovered in a week.

Family history. One grandson had Bell's palsy at the age of 21 from which he recovered. No cases of lingua plicata were found among the relatives.

Examination.—Build and intelligence were normal. The lower lip was twice normal size, with a normal surface. The tongue was large and scrotal, with five sessile papillomata on the dorsum, and a white adherent membrane covering the dorsum and extending slightly over the edges. The buccal mucosae were thickened and showed a patchy adherent white membrane.

A rather superficial biopsy of the lip showed aggregates of plasma cells in the papillary layer of the corium.

Progress.—Meticorten was given orally in doses of 10 mg. *t.i.d.* and reduced gradually until 5 mg. *t.i.d.* was reached after a month. After three months the lip and tongue were normal in size, three of the papillomas had disappeared and most of the white membrane was gone. There was no dribbling or discomfort. With maintenance doses of 5 mg. *b.d.* the patient was apparently normal after 6 months.

Comment.—Dr. F. P. Scott tells me he saw a similarly favourable result from cortisone treatment of this condition in Amsterdam. Schuermann has also noted familial Bell's palsy, epiphora and pyramidal tract lesions in these cases.

Chromoblastomycosis.—Dr. G. H. FINDLAY.

White male, aged 51 years. Four years ago, while loading paraffin tins in a dusty rural environment, he was bruised by one falling on his left forearm. A slowly enlarging warty growth began at the spot, healing in places and extending in others. It had not responded to penicillin injections.

On examination the lower half of the forearm and part of the hand were covered

with a serpiginous, warty, infiltrative eruption which had healed with thin scars in places.

The Wassermann reaction was negative, and histological examination showed a subepidermal granuloma with pseudo-epitheliomatous change over it. The typical brown bodies of chromoblastomycosis were seen in the section, and *Hormodendrum* species was isolated in culture of the tissue.

The lesions were desiccated with the high frequency current and curetted with a sharp spoon. One year later there was only a thin supple scarring of the treated areas with no sign of relapse.

Zosteriform Eruptive Granulomas from a Mycotic Aneurysm.—Dr. F. P. SCOTT.

White female, aged 34. She was delivered of a healthy child two years before, following which there was continued postpartum haemorrhage requiring blood transfusion four weeks after delivery. Three days after transfusion she developed a rash over the left shoulder region which disappeared, leaving one persistent pea-sized nodule on the back of the neck. The nodule was cauterized five months later, but it relapsed and new nodules erupted in the vicinity on the left side over the upper border of the trapezius muscle.

Examination.—Zosteriform arrangement of multiple papules, pinhead to pea size, red-brown in colour, spreading from the mid-line of the neck behind, over the left shoulder and to the supraclavicular region on the left. Pinhead haematomata were present in the zone as well. One papule was examined histologically and the rest destroyed with the electro-cautery. The rash in the zone continued to break out and the new eruption was also examined microscopically.

Progress.—Two months after the first examination a doubtfully pulsating mass, pigeon's-egg size, was found above the left clavicle. It was possibly overlooked before. This was removed and found to be an aneurysm of the transverse cervical artery containing a partly organized mural thrombus. After removal of the aneurysm, no further eruption took place. One year later there was still no recurrence.

Investigations.—Kolmer, negative; blood count and sedimentation rate, normal; x-ray chest, normal; gynaecological examination, normal; no focus of sepsis discovered on general examination.

Histology.—Three papules examined showed well demarcated highly vascular chronic granulomas in the upper corium, resembling granuloma pyogenicum. There were no polymorphs however and no important epidermal involvement. Section of the aneurysm of the artery showed an organizing thrombus without evidence of periarteritis nodosa.

Comment.—A zosteriform eruption on the side of the neck resembling granuloma pyogenicum was evidently produced by emboli from an aneurysm of the transverse cervical artery. The only possible source for the aneurysm itself was puerperal sepsis.

There was however no clinical or cardiographic evidence to suggest patent foramen ovale and consequent paradoxical embolism.

Lipoid Proteinosis (four cases).—Dr. C. M. ROSS.

CASE 1.—White male, aged 35.

His voice became hoarse before puberty and his rash began at 17. At 20 years he was accepted for Air Crew Services but two years later became so dyspnoeic that a tracheotomy was done.

Family history.—His two sisters are affected (Cases 2 and 3). His two children, aged 5 and 3 are well. His parents and grandparents were healthy and unrelated, but one of his maternal grandfather's sisters was blind from birth and very hoarse.

and one of his brothers was blind from birth and suffered repeated attacks of parotid obstruction. His maternal great grandparents were full cousins.

CASE 2.—Married white female, aged 46. (Sister of Case 1.)

From birth she has had lesions on the elbows and a hoarse voice. At the age of 36 her hair became sparse and at 44 she developed nodules on the margins of her eyelids. Despite repeatedly negative serological findings she has received many courses of antisyphilitic treatment, and when first seen was convinced that she suffered from that disease. She has two normal children.

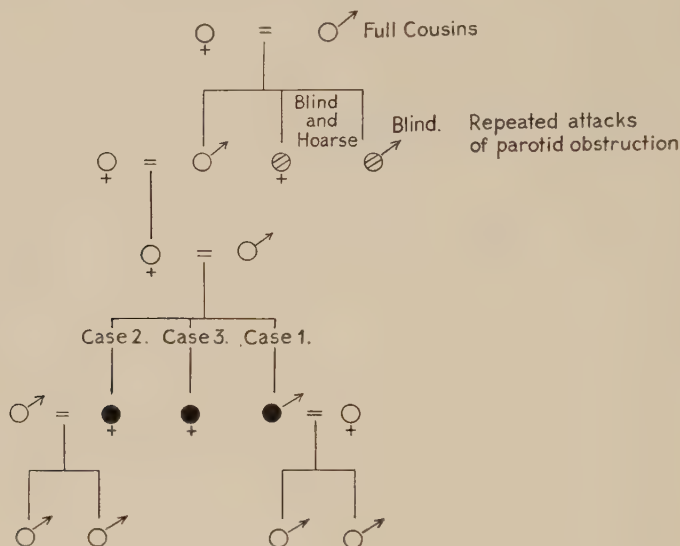


FIG. 1.

CASE 3.—Unmarried white female, aged 43 (sister of Case 1).

She has been hoarse from birth and thinks that her skin lesions were also present then.

CASE 4.—Unmarried white female, aged 33.

This patient states that her hoarseness, her skin lesions and the nodules on her eyelids did not appear until she was 33, though at the age of one she had an attack of diphtheria, after which she lost her voice for some months and at the same age "was covered in sores".

Family history.—This patient is unrelated to the previous three cases.

Her father and mother are healthy and were unrelated. Her seven siblings are healthy.

Comment.—The four cases were clinically and histologically typical of previous descriptions of the disease. None showed abnormality of the blood sugar or blood count or serological evidence of syphilis. In Case 2 the total lipoids, free cholesterol, tot alcholesterol, beta lipo-proteins and alpha lipo-proteins were within normal limits as were the total lipoids in Case 4.

In addition to the usual clinical features, Case 1 showed many soft raised brown plaques, clinically resembling seborrhoeic warts in the axillae, great thickening, redness and infiltration of the upper end of the natal cleft, yellowish follicular infiltrates around the scrotal hairs and an absence of sweating from the face. Case 2 showed marked hypotrichosis with patches of alopecia due to the replacement of hair follicles by plaques of infiltrate, and Case 3, dryness, scaliness and fissuring of

the fingertips. In Case 4 there was a suggestion of wartiness on the knees as well as on the elbows.

When the cases were discussed, it became evident that seven other cases had been seen by those present among the $2\frac{1}{2}$ million whites in South Africa—an incidence of at least 1 in 230,000. No cases had been seen amongst the other races. Cockayne (1933) states that the disorder is a recessive due to a single gene and that in every case the parents and all known relatives have been normal. Although the grand uncle and grand aunt of the first group of cases could not be examined, hoarseness and parotid obstruction, from which they suffered, have been noted in other descriptions of the disease (Sulzberger, 1942) and it is possible that they were affected.

An attempt to treat Case 2 by infiltrating one of the affected areas on her elbow with heparin (5000 units weekly for six weeks) and another area with lipocaic, according to the method of Tompkins and Weinstein (1954), was unsuccessful. There was likewise no response to cortisone by mouth or testosterone by injection.

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CURRENT LITERATURE.

INTRADERMAL TESTS IN THE DIAGNOSIS OF LYMPHOGRANULOMA VENEREUM. A. J.KING, C. F. BARWELL and R. D. CATTERALL. (1956) *Brit. J. vener. Dis.*, **32**, 209.

Routine intradermal tests with a yolk sac antigen of lymphogranuloma venereum virus were applied to 1317 patients attending a venereal diseases clinic for the first time. Positive tests were found in 206 cases (18.4%). In 23 of those cases (2% of the total) the diagnosis of lymphogranuloma venereum was confirmed by strongly positive complement fixation tests although only 10 of these patients were found to have clinical evidence of the disease. A much larger number of patients, namely 157, showed complement fixation antibodies in the blood serum but not in sufficient quantity to justify a diagnosis of active disease. The findings suggest that there is an appreciable incidence of undiagnosed lymphogranuloma venereum in the population of the East End of London.

W. G. A.

LATE HEPATIC SYPHILIS. I. A. KELLOCK and S. M. LAIRD. (1956) *Brit. J. vener. Dis.*, **32**, 236.

The incidence, clinical manifestations, diagnosis, treatment and prognosis of late hepatic syphilis are discussed and six probable cases are described. The authors recommend that in all cases presenting with hepatic enlargement syphilis should be considered and serological tests conducted. They conclude by stating that a positive therapeutic test is most probably the most valuable single procedure in confirming the association between syphilis and liver enlargement, with penicillin as the drug of choice.

W. G. A.

OSSEOUS LESIONS IN URTICARIA PIGMENTOSA. F. G. ZAK, J. A. COVEY and J. J. SNODGRASS.(1957) *New Engl. J. Med.*, **256**, 56.

A woman aged 58 with urticaria pigmentosa had a large liver and in the bones, especially those of the spine ribs and pelvis, were abnormal areas, some of which were denser and others less dense than is usual.

Biopsy of the iliac crest showed non-granular mono-nuclear cells replacing normal marrow. These cells were thought to be either immature or post-mature mast-cells.

A. D. P.

STUDIES OF BESNIER'S PRURIGO. S. HELLERSTROM and H. LIDMAN. (1956) *Acta dermat. venereol., Stockh.*, **36**, 11.

One-sixth to one-fifth of all patients in the Dermatological Clinic of the Karolinska Institute suffer from Besnier's prurigo. The authors believe there is an absolute increase, due probably to increasing numbers of sensitizing agents. They regard these patients as "real sensitization machines".

O. L. S. S.

THE CLINICAL PICTURE AND PATHOGENESIS OF SCLEROMYXOEDEMA. E. KEINING and O. BRAUN-FALCO. (1956) *Acta dermat. venereol., Stockh.*, **36**, 37.

A case is described in clinical and histological detail. The mucinous deposits vary with different forms of "myxoedema" for the cutaneous forms, e.g. myxoedema lichenoides. The nature of the pathology of scleromyxoedema is discussed.

O. L. S. S.

IS PEMPHIGOID A SEPARATE DISEASE ENTITY? F. MIEDZINSKI and A. NIEDZWIEDZKA. (1956) *Acta dermat. venereol., Stockh.*, **36**, 72.

A case is described, and the clinical picture of the disorder is considered. The authors believe that the answer is YES.

O. L. S. S.

HUMORAL CHANGES IN SEBORRHOEA. D. O. PIERINI and E. S. BREARGGER. (1956) *Arch. argent. Derm.*, **6**, 153.

After investigating 16 patients with seborrheic alopecia and 6 with acne vulgaris the authors conclude:— (1) The blood lipoids are usually increased at the expense of the fatty acids and, to a lesser degree, of cholesterol, although there are great individual variations. (2) All patients investigated had a moderate degree of hypovitaminosis A.

G. W. B.

LIPOID PROTEINOSIS—PORPHYRIA. J. M. BORDA, J. ABULAFIA and A. I. CARVALHO. (1956) *Arch. argent. Derm.*, **6**, 239.

About 40 examples of lipid proteinosis have been recorded, but the types of lesion in the skin have varied considerably from patient to patient; very few of them are common to all patients; pigmentation, often near the angles of the mouth, is one, and papules especially along the margin of the upper eyelid is another.

The authors describe 3 patients with typical porphyria, none of them with a family history of it, in whom they found lesions that were clinically, histopathologically and histochemically identical with those found in lipid proteinosis. Their detailed study of the recorded cases of the latter makes it obvious that many of the lesions described could equally well be those of porphyria. Diabetes may supervene in both affections, so the underlying metabolic disturbance in both must be very closely related; it concerns the catalytic action of tetrapyrrol pigments on unsaturated fatty acids.

Pseudo-colloid milium is probably due to a similar metabolic derangement.

G. W. B.

MALIGNANT MELANOMA. S. CADE. (1957) *Brit. med. J.*, **i**, 119.

An important account based on 132 patients treated at Westminster Hospital. Treatment is discussed fully. The initial treatment is vitally important as minor excisions, biopsies, or other interference result in a negligible chance of survival.

S. T. A.

ACUTE SCHÖNLEIN-HENOCH PURPURA TREATED WITH PREDNISOLONE. A. S. COHEN. (1957) *Brit. med. J.*, **i**, 143.

A 10-year-old girl treated with apparent success after no response to cortisone.

S. T. A.

MYOPATHY IN SHEEP. F. D. BOSANQUET, P. M. DANIEL and H. B. PARRY. (1956) *Lancet*, **ii**, 738.

Whether this hitherto unrecorded myopathy in sheep is as closely related to dermatomyositis as the authors suggest or not, it is of great interest to dermatologists because of the association of skin changes with muscle degeneration. The skin changes consist of papules in the woolled and haired areas and often swelling and oedema of the skin over the dorsal nasal bones. The histological changes in the muscle consist of primary degeneration affecting skeletal muscles and sometimes the myocardium. Scattered foci of small round cells may occur in the muscles. The disease is usually fatal.

R. H. M.

LUPUS VULGARIS TREATED WITH ISONIAZID. BRIAN RUSSELL and N. A. THORNE. (1956) *Lancet*, **ii**, 808.

The treatment of 111 patients suffering from lupus vulgaris with isoniazid is described. Ninety-nine patients were clinically clear after treatment and of these only 11 have relapsed. The authors suggest that the dose of isoniazid should be 300 mg. daily up to at least three months after clinical cure. They have not found it necessary to give streptomycin with isoniazid or to use any form of local therapy including the Finsen-Lomholt and Kromayer lamps, except occasionally acid nitrate of mercury to destroy solitary nodules.

One case of tuberculosis verrucosa cutis, three of scrofuloderma and two of erythema induratum all responded satisfactorily to this treatment while one patient with acne agminata did not improve.

R. H. M.

HYPERCALCAEMIA DUE TO SARCOIDOSIS. R. R. MCSWINEY and I. H. MILLS. (1956) *Lancet*, **ii**, 862.

Two patients with sarcoidosis, hypercalcaemia and impairment of renal function were treated with cortisone. This produced a fall in plasma calcium and phosphorus. Renal function improved when the plasma calcium level fell. Hypercalcaemia appears to be a rare complication of sarcoidosis and it has been suggested that this is the chief cause of renal impairment in sarcoidosis. Hypercalcaemia is not related to hyperproteinaemia and it must only very rarely be due to bone erosion by sarcoid deposits. Patients with sarcoidosis may overact to vitamin D and thus produce hypercalcaemia. The authors do not mention the liability of patients with sarcoidosis to develop

considerable hypercalcaemia and toxic signs if treated with calciferol, supporting the hypothesis that such patients may react more to vitamin D than normal. R. H. M.

CONJUNCTIVITIS AND EYELID ECZEMA DUE TO HYPERSENSITIVENESS TO ADRENALIN SOLUTION EMPLOYED IN SPRAY-TREATMENT OF ASTHMA. HELGE COLLDALH and ERIK FACEBERG. (1956) *Acta allergol.*, **10**, 77.

An asthmatic using a spray containing adrenalín developed conjunctivitis and oedema of the eyelids. Symptoms subsided soon after discontinuing the spray. Patch tests gave a positive reaction to 10% adrenaline but negative ones to the other ingredients. No reaction was given to adrenaline by other asthmatic patients. H. T. H. W.

THE AETIOLOGY OF ACRODERMATITIS CHRONICA ATROPHICANS (PICK-HERZHEIMER). A. MARCHIONINI. (1956) *Ann. Derm. Syph. (Paris)*, **83**, 601.

The author describes the classical features of the disease and the various theories of its causation—infection, endocrine abnormality, congenital vulnerability of the elastic tissue, etc. The favourable response of early cases to penicillin suggests an infective origin. In support of this are the successful transmissions of the condition to normal people carried out by Götz in the author's clinic. Unfortunately all attempts to identify an infectious agent were negative whether for bacteria, a virus or a spirochete. F. F. H.

GENODERMATOSES WITH VARYING RINGED ERYTHEMA. A. BAZEN and A. DUPRÉ. (1956) *Ann. Derm. Syph. (Paris)*, **83**, 612.

A woman aged 49, from the first weeks of life had presented 3 types of lesions:—(1) Varying ringed erythema, the whole body being covered with little pink macules with a scaly collarette, gradually spreading centrifugally and eventually fading in 1 to 3 weeks. (2) Fixed peri-orificial erythema. (3) Hypotrichosis with scanty hair on the scalp. They believe that the condition is one of a group of related genodermatoses, which include "erythrokeratoderma variabilis" (Mendes da Costa) "genodermatose en coqueret" (Degos) and certain forms of ichthyosiform erythrodermia. F. F. H.

THE MACULAR ANETODERMIS. R. DELUZENNE. (1956) *Ann. Derm. Syph. (Paris)*, **83**, 618.

This is a useful survey of the history, clinical and histological features of macular atrophies based on some 200 cases culled from the literature. The author suggests the following classifications:
A. Primary anetodermia. (1) Cryptogenic. (2) Associated with some general condition.
B. Anetodermia secondary to some local disease. This may be syphilis or tuberculosis, urticarial or purpuric lesions. F. F. H.

PAPULAR ERUPTION OF THE BACK DURING THE COURSE OF LUPUS ERYTHEMATOSUS. P. DE GRACIANSKY, J. HEWITT, S. BOULLE and R. LECLERCQ. (1956) *Ann. Derm. Syph. (Paris)*, **83**, 636.

A patient with lupus erythematosus developed an eruption on the face which became bullous and crusted, and also little rounded papules on the back, 1 cm. in diameter, looking almost like urticarial papules. The first attack responded to cortisone and vitamin E, and a second one to nivaquin. They believe these lesions are the same as those described by Gold and indicate activity in the disease. Histologically, the most significant change is in the ground substance. F. F. H.

DERMATOLOGICAL OCCUPATIONAL DISEASES. H. TH. SCHREUS. (1956) *Berufsdermatosen*, **4**, 201.

Schreus sees a rise in industrial disease of which skin disease forms 4% of the total. For the sake of non-dermatological industrial and factory doctors the exact differentiation and nomenclature of the eczemas whether contact or not would be highly desirable. German practice as regards compensation and possibilities of change of job without leaving work entirely are discussed. M. F.

SYSTEMIC TOXIC EFFECTS FROM CHLORACNE-PRODUCING SUBSTANCES. W. SCHMIDT and W. BOSLET. (1956) *Berufsdermatosen*, 4, 214.

Twelve patients who had chloracne were followed up and four had gastric or duodenal ulcer, one cirrhosis of the liver and others non-specific gastric complaints. M. F.

INFLUENCE OF OCCUPATION ON ENDOGENOUS ECZEMA. O. FUCHS. (1956) *Berufsdermatosen*, 4, 225.

Because, in a series of 578 cases, textile workers were most frequent a susceptibility to wool or wool dust is deduced. M. F.

ROLE OF LIGHT IN OCCUPATIONAL DERMATOSES. H. IPPEN. (1956) *Berufsdermatosen*, 4, 235.

A reminder about photosensitizing properties of furocoumarines, phenothiazines, tars etc.

M. F.

PSORIASIS AND ACCIDENT. G. WEBER. (1956) *Berufsdermatosen*, 4, 242.

The relationship is possibly worth discussing because the isomorph scratch reaction would present a medico-legal problem. M. F.

ANTIBIOTICS AS OCCUPATIONAL ALLERGENS IN THE PHARMACEUTICAL INDUSTRY.

H. E. KLEINE-NATROP. (1956) *Berufsdermatosen*, 4, 269.

Patch tests in a factory showed 6.2% +ve to penicillin, 1.0% to tetracycline, 2.6% to streptomycin and 0.2% to a tyrothricin-xanthocillin combination. M. F.

DERMATOMYOSITIS: UNUSUAL FEATURES, COMPLICATIONS AND TREATMENT. HERBERT

B. CHRISTIANSON, LOUIS A. BRUNSTING and HAROLD O. PERRY. (1956) *Arch. Derm. Syph., Chicago*, 74, 581.

The authors found from a study of the records of 270 patients that the ratio of females to males was 2:1, that in only one instance was more than one member of the family affected, that association with malignant disease (6.7%) was coincidental, that in two patients Cushing's syndrome was present, in two L.E. cells were found in the blood, in two pityriasis rubra pilaris-like eruptions were found, gastro-intestinal symptoms were common, calcinosis was present in 29.1% and osteoporosis in 21.8% but were apparently unrelated. Prolonged administration of steroids seems well worth while. J. K.

THE MOTHER-CHILD RELATIONSHIP IN THE GENESIS OF NEURODERMATITIS. JUDD

MARMOR, MILTON ASHLEY, NORMAN TABACHNICK, MARGARET STORKAN and FRANKLIN McDONALD. (1956) *Arch. Derm. Syph., Chicago*, 74, 599.

The mother-child relationship of 22 children with infantile eczema was studied, and it was found that neglect or too rough or insufficient handling of the child was present in all cases. Psychological studies of 10 of the mothers showed that they were all emotionally immature. (Personal experience hardly bears the above statements out. Frequently the patient is a cheerful, chubby, well-cared-for child and the mother at least of average intelligence and emotional maturity.) J. K.

DERMABRASION WITH RASPS. DOUGLAS TORRE. (1956) *Arch. Derm. Syph., Chicago*, 74, 615.

This, the latest method of treating acne scarring, consists of abrasion with sculptors' rasps and similar instruments under local anaesthesia. The method is slower than others but is simpler, cheaper and less liable to mishap. J. K.

THE DISTRIBUTION OF ALKALINE PHOSPHATASE IN NORMAL AND PATHOLOGIC SKIN.

ALFRED W. KOPF. (1957) *Arch. Derm. Syph., Chicago*, 75, 1.

This prize-winning essay is the result of extensive study of the literature (there are 195 references) and original observation of alkaline phosphatase in the skin. Normally alkaline phosphatase activity is found in hair papillae and connective tissue sheath of hair follicles, sweat glands and in the capillaries. In disease it is found where there is active vascular proliferation or in banal inflammatory dermatoses, in early phases of connective tissue proliferation or in benign neoplasms where the parent tissue shows such activity. Malignant tumours show variable alkaline phosphatase activity. J. K.

ULTRAVIOLET LIGHT IN CHLORPROMAZINE DERMATITIS. MILTON M. CAHN. (1957) *Arch. Derm. Syph., Chicago*, 75, 38.

"Only intense summer sunlight in areas relatively free of smoke or dust appeared to contain those rays necessary to induce dermatitis" in 5 patients suffering from Largactil light sensitization. J. K.

LUPUS ERYTHEMATOSUS: ENLARGEMENT OF THE PAROTID GLAND. OSWALDO G. COSTA. (1957) *Arch. Derm. Syph., Chicago*, 75, 41.

Since Kaposi's original observation very few cases of parotid swelling complicating lupus erythematosus have been recorded. It appears to be a true complication and not a separate affection. J. K.

DERMATOHISTOPATHOLOGY OF VARIOUS TYPES OF SCLERODERMA. PAUL A. O'LEARY, HAMILTON MONTGOMERY and WILLIAM E. RAGSDALE, JR. (1957) *Arch. Derm. Syph., Chicago*, 75, 78.

The authors have adopted O'Leary's classification of scleroderma: I. Generalized; (A) diffuse type, (B) acrosclerosis and II. Localized; (A) morphoea either localized or generalized where the patches are numerous, and (B) other types, linear or localized forms associated with hemiatrophy. Linear or other localized forms may precede or be associated with hemiatrophy or be associated with congenital defects in children. The generalized forms do not occur before puberty.

In diffuse generalized scleroderma there is greater increase in the thickness of the cutis and more fibrosis of the subcutaneous tissue than in the localized forms; but in acrosclerosis there is thinning of the cutis and atrophy of the collagen is more prominent. Obliterative changes in the vessels are minimal in morphoea and greatest in diffuse scleroderma. In all forms there is increased melanin pigment in the basal layer. Distinction between the different forms is important if only in regard to prognosis. J. K.

CYCLOHEXAMID (ACTIDION) AGAR, AN ADVANCE IN THE CULTURE OF DERMATOPHYTES. F. FEGELER. (1956) *Dermatologica*, 113, 65.

Selective media have long been used to suppress the growth of contaminating bacteria, but only recently has an antibiotic been found that suppresses moulds, while permitting growth of pathogenic fungi. This is Actidion, later called Cyclohexamid, a product of *Streptomyces griseus*. Its incorporation in a glucose-agar medium, together with penicillin and streptomycin, has given many more successful results in the isolation of dermatophytes from heavily contaminated material. It has the additional advantage of eliminating false diagnoses of scopulariopsidosis, candidiasis, etc. J. F. S.

PSORIASIS AND STRESS. F. REIS. (1956) *Dermatologica*, 113, 71.

Reiss emphasizes the part played by "stress" in the pathogenesis of psoriasis, and under this term he includes infections, chemical or radiation injury, hypersensitivity towards foods or drugs, and also emotional or hormonal disturbances. Partial success in some cases with chlorpromazine supports his belief in the importance of psychological factors. Both his premisses and his logic are open to criticism, but there may nevertheless be some substance in his conclusions. J. F. S.

EXTERNAL FACTORS IN THE AETIOLOGY OF PORPHYRIA CUTANEA TARDA AND OF DIABETES MELLITUS. J. BERMAN and T. BIELOCKY. (1956) *Dermatologica*, 113, 78.

The significance of external factors in the pathogenesis of p.c.t. was investigated in 36 patients, 34 men and 2 women. Chronic alcoholism was found in all but one: 16 of them (44.4%) admitted to have had syphilis formerly, but owing to intensive treatment, only one was still sero-positive: diabetes was found in 15 patients (41.7%). Among 1250 male diabetics 1.0% were found to have p.c.t., while among 1430 female diabetics none were found. In patients with a history of syphilis, the incidence of diabetes was twice as high as among syphilis-free persons. These two complaints should therefore always be looked for. From their findings, the authors consider that external factors, especially those that damage the liver, are more important than inherited factors. The discovery of porphyria in 8 patients who as yet had no skin changes proved further that not only in acute porphyria, but also in p.c.t., there is a latent form. (Modified from author's summary.) J. F. S.

CONTACT DERMATITIS FROM NEOMYCIN DUE TO DERMAL DELAYED (TUBERCULIN-TYPE) SENSITIVITY. S. EPSTEIN. (1956) *Dermatologica*, 113, 191.

Ten cases of dermatitis from contact with neomycin apparently were due to delayed dermal sensitivity (tuberculin-type) and not to epidermal sensitivity. These cases can easily be overlooked, because neomycin dermatitis of this type often appears just as an aggravation of the pre-existing condition, rather than as an easily recognized acute secondary contact dermatitis. Furthermore, patch-tests are often negative or only inconstantly positive, and preparations containing a combination of neomycin and hydrocortisone may temporarily appear beneficial. However, intradermal tests with neomycin are always positive in these cases. As this form of neomycin contact sensitivity appears to occur frequently, attention is drawn to it. In cases of suspected sensitivity to neomycin with negative patch-tests, intradermal tests with a 1:1000 or 1:100 dilution of neomycin are suggested. (Slightly modified from author's summary.)

J. F. S.

HYPERKERATOSIS PALMO-PLANTARIS WITH PERIODONTOSIS. (PAPILLON-LEFÈVRE).

L. H. JANSEN and G. DEKKER. (1956) *Dermatologica*, 113, 207.

The authors discuss three types of inherited hyperkeratosis of palms and soles, namely, "Mal de Meleda", which is recessive; keratoma hereditarium palmare et plantare (Unna-Thost), which is a regular dominant; and hyperkeratosis palmo-plantaris with periodontosis (Papillon-Lefèvre), which is recessive. They describe a fresh case of the last type, a girl of 10, whose parents were first cousins, but in whose family no other member was known to be affected. The dental changes were severe, and from the literature it appears that all teeth may be lost at an early age. Biopsy of the sole in their case showed parakeratosis as well as hyperkeratosis, and this feature serves further to mark off this type from the others. Although the authors have discussed only these three groups, they recognize that there are other varieties.

J. F. S.

ERYTHEMA AXILLARUM PERSTANS OF MICROCOCCAL ORIGIN. A. CASTELLANI. (1953) *Dermatologica*, 113, 202.

An account of four cases of a persistent erythematous eruption in the axillae, from which the author isolated a peculiar micrococcus, which on glucose-agar and other media produced a vivid violet pigment. The patients were all American seamen, who were thought to have acquired the infection in the West Indies. They had no subjective symptoms. One patient showed in addition slight affection of his finger-tips, and another a patch on an antecubital fold. Treatment proved rather unsatisfactory, the author's well-known fuchsin paint being about the most successful application. There follows a full technical description of the micrococcus, with a coloured plate of a culture.

J. F. S.

HYALURONIC ACID INVESTIGATIONS IN LOCAL MYXOEDEMA AND IN THE STROMA OF SKIN CANCERS. J. LENGYEL and B. VERTES, (1956) *Dermatologica*, 113, 219.

After observing very high concentrations of hyaluronic acid in the corium in a case of myxoedema circumscriptum, the authors investigated this point in the stroma of skin cancers, by means of metachromatic staining, with the interesting finding that hyaluronic acid was abundant in the stroma of basal-celled epitheliomata, but almost absent from that of spinocellular cancers. They suggest that the acid is an important defence substance in the stroma.

J. F. S.

CHRONIC LUPUS ERYTHEMATOSUS OF THE CONJUNCTIVA. X. VILANOVA, C. CARDENAL and J. M. CAPDEVILA. (1956) *Dermatologica*, 113, 226.

Description of two cases in which the tarsal conjunctiva was affected in chronic L.E. The authors think that it is probably not very uncommon.

J. F. S.

APOKRINE SWEAT RETENTION IN MAN. IV. THE "FOAM CELL" REACTION TO THE ESCAPE OF APOKRINE SWEAT INTO THE DERMIS. W. B. SHELLEY and M. M. CAHN. (1955) *J. invest. Derm.*, 25, 169.

This phenomenon was observed in the course of experiments in poral closure and, though it is said to be a prominent finding in cystic disease of the breast, it is not known to occur spontaneously in the skin. It is a function of the histiocytes and it can also be elicited by the intradermal injection of milk.

J. H. T. D.

AUGMENTED PIGMENTATION AND OTHER RESPONSES OF NORMAL HUMAN SKIN TO SOLAR RADIATION FOLLOWING ORAL ADMINISTRATION OF 8-METHOXYPSORALEN.

T. B. FITZPATRICK, C. E. HOPKINS, D. D. BLICKENSTAFF and S. SWIFT. (1955) *J. invest. Derm.*, **25**, 187.

Though an earlier investigation had appeared to show that MOP ingested 3 hours before exposure improved the tolerance of U.V.L. and diminished the erythema, this field trial performed on inmates of Arizona State Prison demonstrates that 50 mg. taken 3 hours before exposure to the sun does in fact augment all cutaneous responses to solar radiation.

J. H. T. D.

STUDIES ON THE DISSEMINATION OF FUNGI FROM THE FEET OF SUBJECTS WITH AND WITHOUT FUNGUS DISEASE OF THE FEET. J. A. ROSENTHAL, R. L. BAER, J. Z.

LITT, H. ROGACHEFSKY and D. FURNARI. (1956) *J. invest. Derm.*, **26**, 41.

While no attempt is made to urge that tinea pedis is readily communicated through fomites, it is shown here that water, in which the feet have merely been soaked for 15 minutes without interdigital friction or even agitation, is very nearly as likely to contain filaments as scrapings made *ad hoc*. Filaments were discovered microscopically also in 12% of the sediments obtained by soaking the feet of subjects having no signs of ringworm. Dermatophytes were isolated by culture on cycloheximide agar 32 times from scrapings, 11 times from sediments and 9 times by both methods, that is to say from 43 of the 91 subjects with clinical ringworm.

J. H. T. D.

THE ROLLER TUBE TISSUE CULTURE TECHNIQUE IN THE EVALUATION OF THE PRIMARY IRRITANCY PRODUCING CAPACITY OF TOPICAL MEDICAMENTS AND CHEMICALS.

H. FUNAN, C. S. LIVINGOOD, and J. F. HILDEBRAND. (1956) *J. invest. Derm.*, **26**, 23.

Eight cu. mm. of preputial epidermis is inoculated into chicken plasma clot on a narrow cover-slip placed in a test tube containing enough nutrient fluid to wet the surface every 5 minutes during 7-14 days incubation, the tube being slowly revolved on its long axis. To the nutrient fluid is added the irritant under investigation.

The answer is expressed in terms of "no injury", "partial injury" and "complete injury" at so many γ per cc. The figures for "no injury" vary from 1 γ of hydrarg. perchlor. and pot bichrom. through various antipruritics and antibiotics at 100-500 γ , boric acid at 8000 penicillin at 10,000 and neomycin 20,000, concentrations which correspond reasonably well with the Rostenberg and Sulzberger list of substances for patch testing.

The method appears to have certain advantages over the hanging drop technique and is here proposed for the purpose of screening new water-soluble substances the use of which in industry might be contemplated. The cytological changes are studied by phase contrast microscopy; but if the ability of the tissue to recover is not in issue, the preparations may be fixed and stained with May-Greenwald and Giemsa.

J. H. T. D.

THE PHYSIOLOGY OF THE APOKRINE (CERUMINOUS) GLAND OF THE HUMAN EAR CANAL.

W. B. SHELLEY and E. T. PERRY. (1956) *J. invest. Derm.*, **26**, 13.

By contraction of the myoepithelium the secretion of the ceruminiferous apocrine gland appears in the lumen either in the form of watery droplets or as a colourless surface film, drying up to form a gummy semi-solid which mixed with sebum and desquamation constitutes cerumen.

The myoepithelium contracts in response to pain, anxiety, clenching of the teeth, local massage or local injection of pitocin, cholinergic drugs, and to a less extent, local anaesthetics. The use of a 30-gauge needle avoids the production of sufficient pain to act as a stimulus in itself. Secretion is supposed to be a continuous process occupying about 3 days to fill the ducts. The remarkable photograph of delivery taking place on the anterior wall of the meatus was secured by an astonishingly simple means of illumination. Photomicrographs illustrate a comparative study of aural and axillary apocrine glands. (It is surely unnecessary and even somewhat confidence-destroying to justify studies of this degree of excellence on the grounds of possible usefulness in the treatment of otitis externa!)

J. H. T. D.

DISRUPTION OF TONOFIBRIL AND INTERCELLULAR BRIDGES BY DISULPHIDE-SPLITTING AGENTS. R. B. SLOUGHLIN and N. NOVAK. (1956) *J. invest. Derm.*, **26**, 127.

A histological study of the epidermolytic effects of heat and cold, cysteine, glutathione and sodium thioglycollate at various temperatures and of the influence of certain enzyme inhibitors.

J. H. T. D.